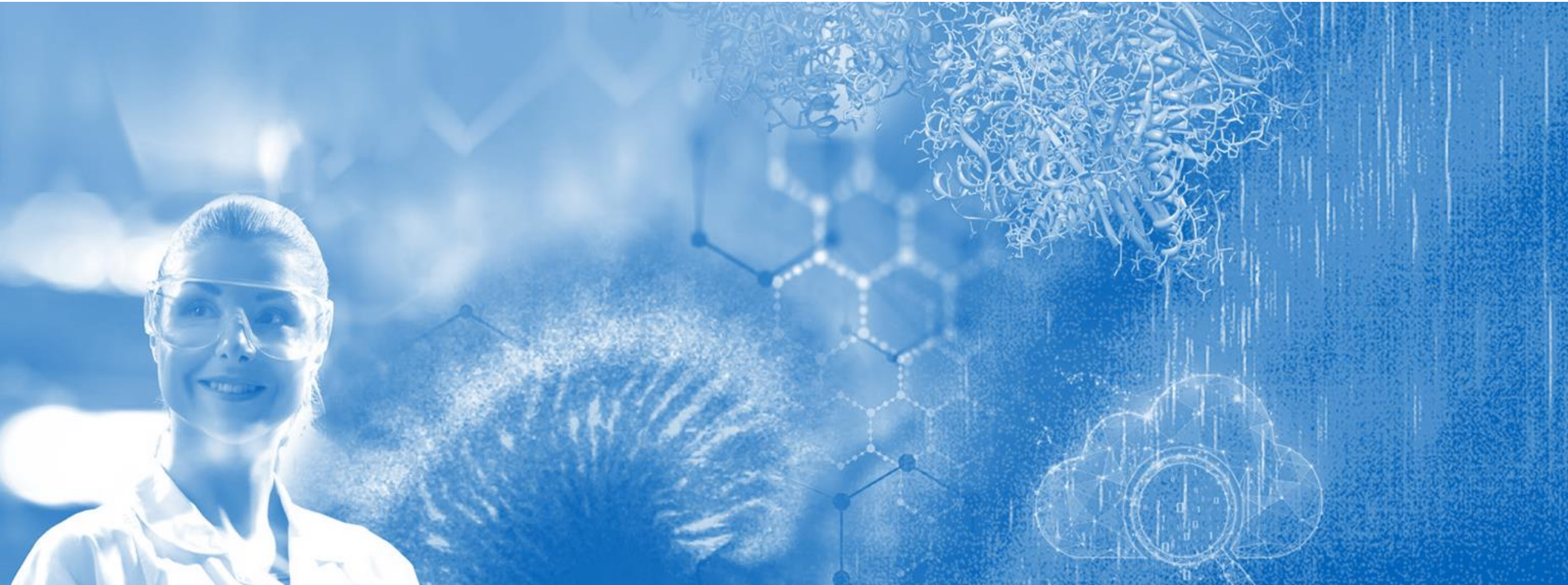
MRMS :
The technology of ultra-high mass resolution and mass accuracy

December 2022

Dr. Matthias Witt
Bruker Daltonics GmbH & Co. KG, Bremen, Germany

Instrumentation



MRMS technique
Not your father's FT-ICR MS

Magnetic Resonance Mass Spectrometry

1973 → 1983 → 2009 → 2013 → 2016 → 2018

- Fourier transform ion cyclotron resonance mass spectrometry *FT-ICR MS* is a technique invented in **1973**.
- Commercially marketed as **FTMS** by Bruker starting in the **mid 80s**.
- Introduction of solariX in **2009**.
- The **ParaCell™** was introduced in **2013** with solariX XR and several generations later, the modern FT-ICR MS was nothing like the ones from 40 years ago.
- Indroduction of solariX 2xR in **2016** with quadrupolar phase detection.
- Since **2018** **MRMS** defines the next generation of instrumentation – *not Orbitrap*. Naming follows **NMR** & **MRI** reflecting ease of use of MR systems.

Bruker's Magnet Technology

NMR, MRI & MRMS: A long history of magnet innovations

Refrigerated Magnet

- 7T, 12T & 15T magnets
- Compact design
- Small stray field
- **No** Liquid Nitrogen
- Extended liquid Helium hold time (290 L Helium once a year)
- Biennial cold-head exchange
- Quench duct required

solarix

Maxwell Magnet

No need for operational cryogens fills ever

- 7T magnet
- Very compact design
- Small stray field
- **No** Liquid Nitrogen
- **No** Liquid Helium fill needed
- Biennial cold-head exchange
- **No** Quench duct required

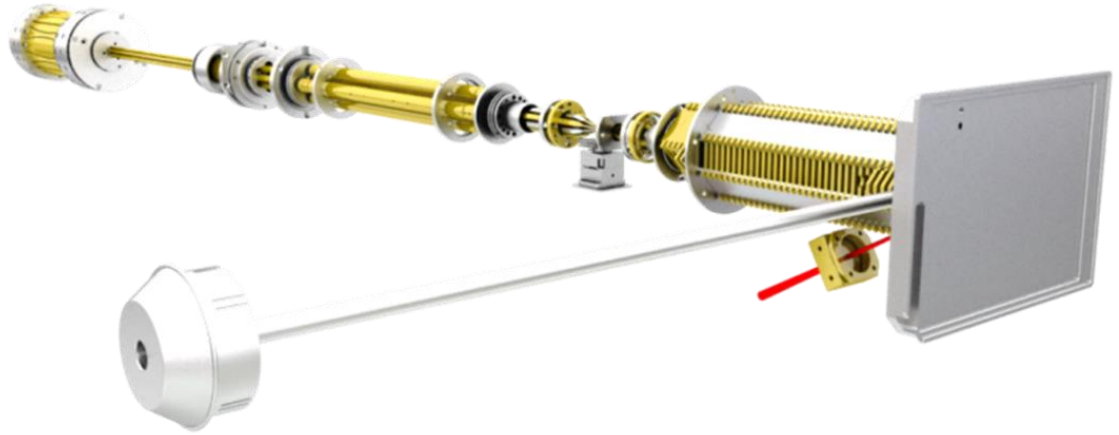
scimaX

Versatility, performance and accuracy all in one platform

scimaX delivers unmatched versatility and unparalleled performance to provide answers with confidence for your most challenging applications

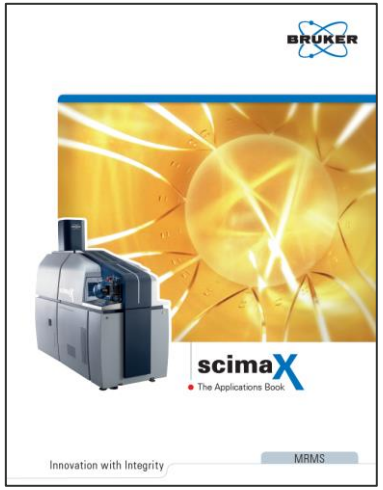
scimaX

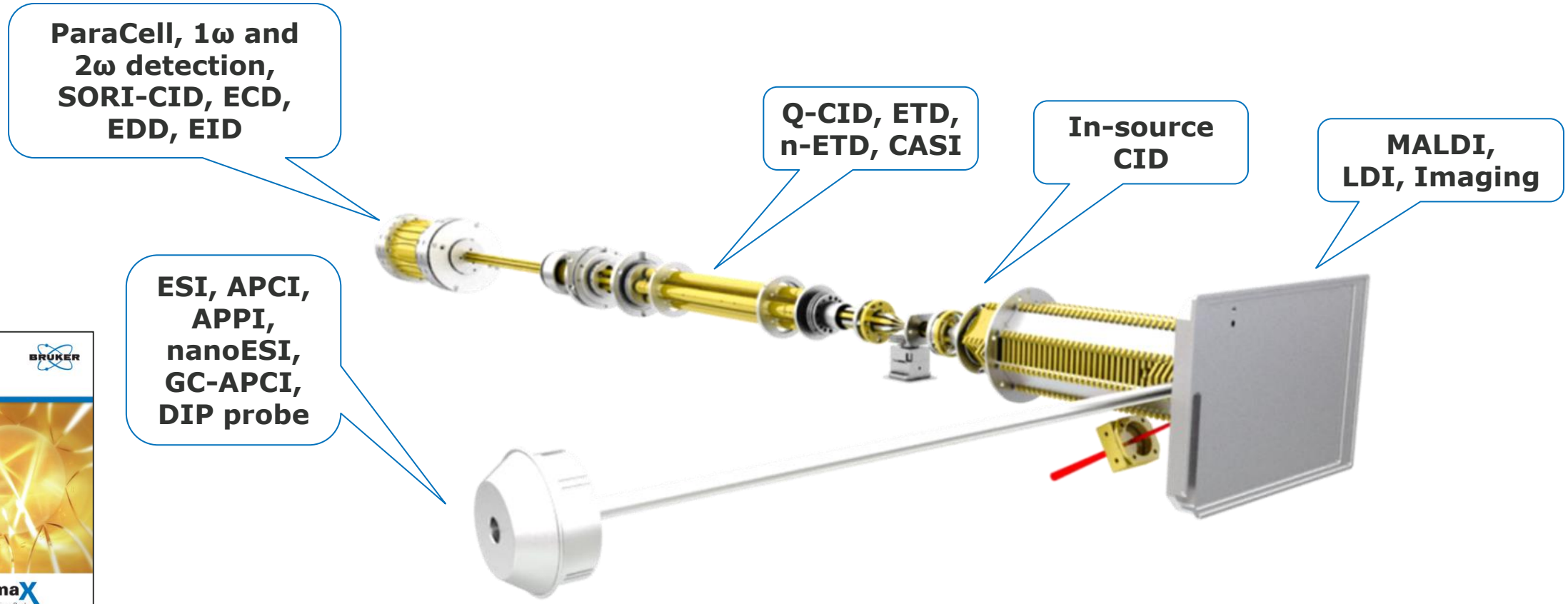
- Molecular imaging of tissues
- In-depth analysis of petroleum products
- In-depth analysis of complex environmental samples
- Comprehensive metabolomics and other life science studies
- Intact protein analysis
- Glycan analysis



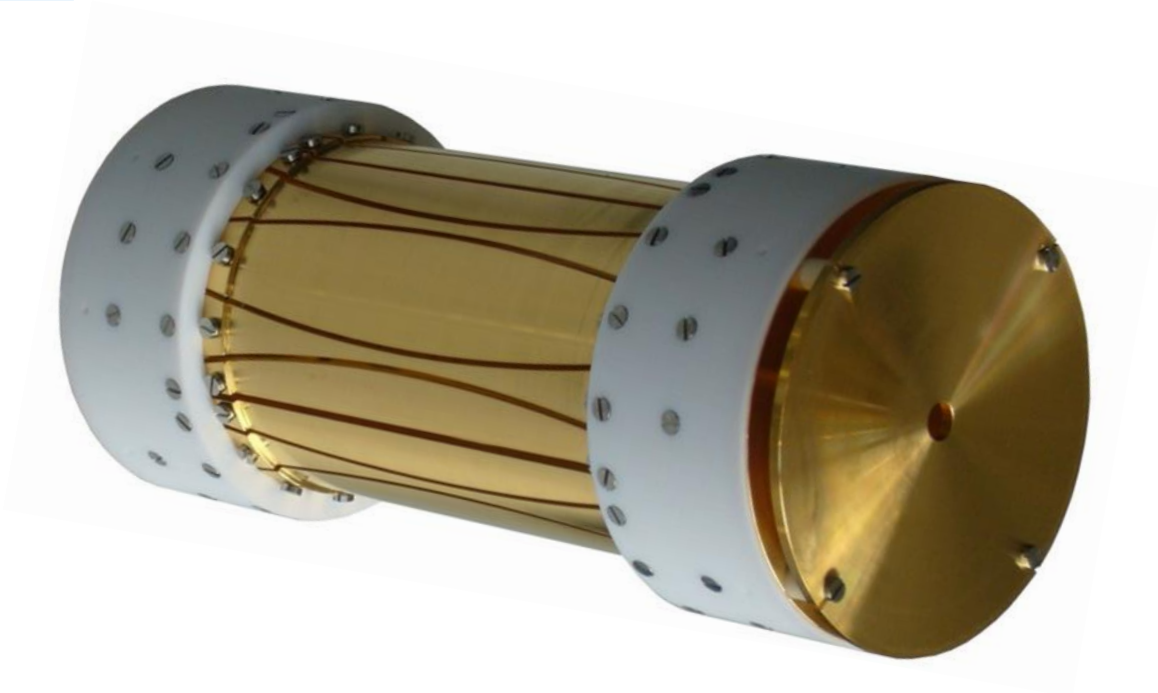
Versatility, performance and accuracy all in one platform

scimaX delivers huge diversity of ionization sources and fragmentation methods





MRMS Detector



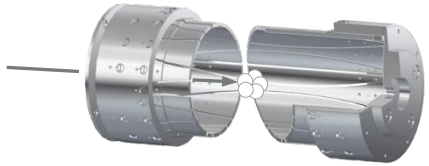
ParaCell XR detector

- Dynamically harmonized ICR cell (DHC): Harmonic, parabolic potential for all cyclotron orbits
- Maximum resolution > 10M already at 7T
- Detector cell for Bruker MRMS
- Detector cell for the NHMFL 21T instrument based on DHC concept

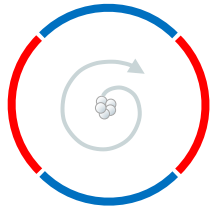
I. A. Boldin, E. N. Nikolaev, *Rapid Commun. Mass Spectrom.*, **25**, 122, (2011)
E. N. Nikolaev, I. A. Boldin, R. Jertz, G. Baykut, *J. Am. Soc. Mass Spectrom.*, **22**, 1125, (2011)

The MRMS experiment

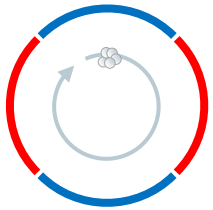
1) Get your analyte in the detector
(Trap ions)



2) Get it ready for measurement
(Excitation)

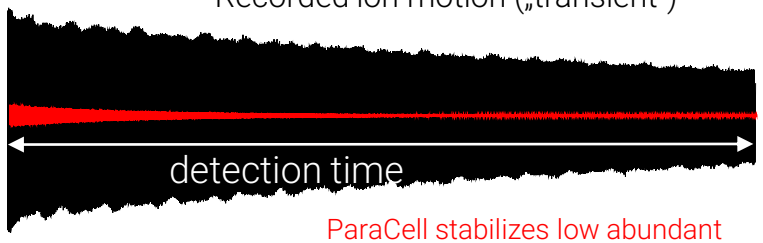


3) Measure your analyte
(Detection)



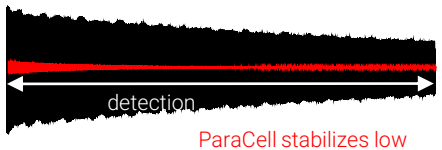
$$\omega_c = \frac{qB}{m}$$

Recorded ion motion („transient“)



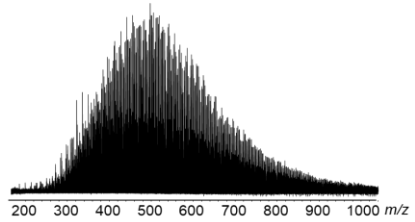
ParaCell stabilizes low abundant ions

4) Get a mass spectrum
(Fourier Transformation (FT) and Calibration)

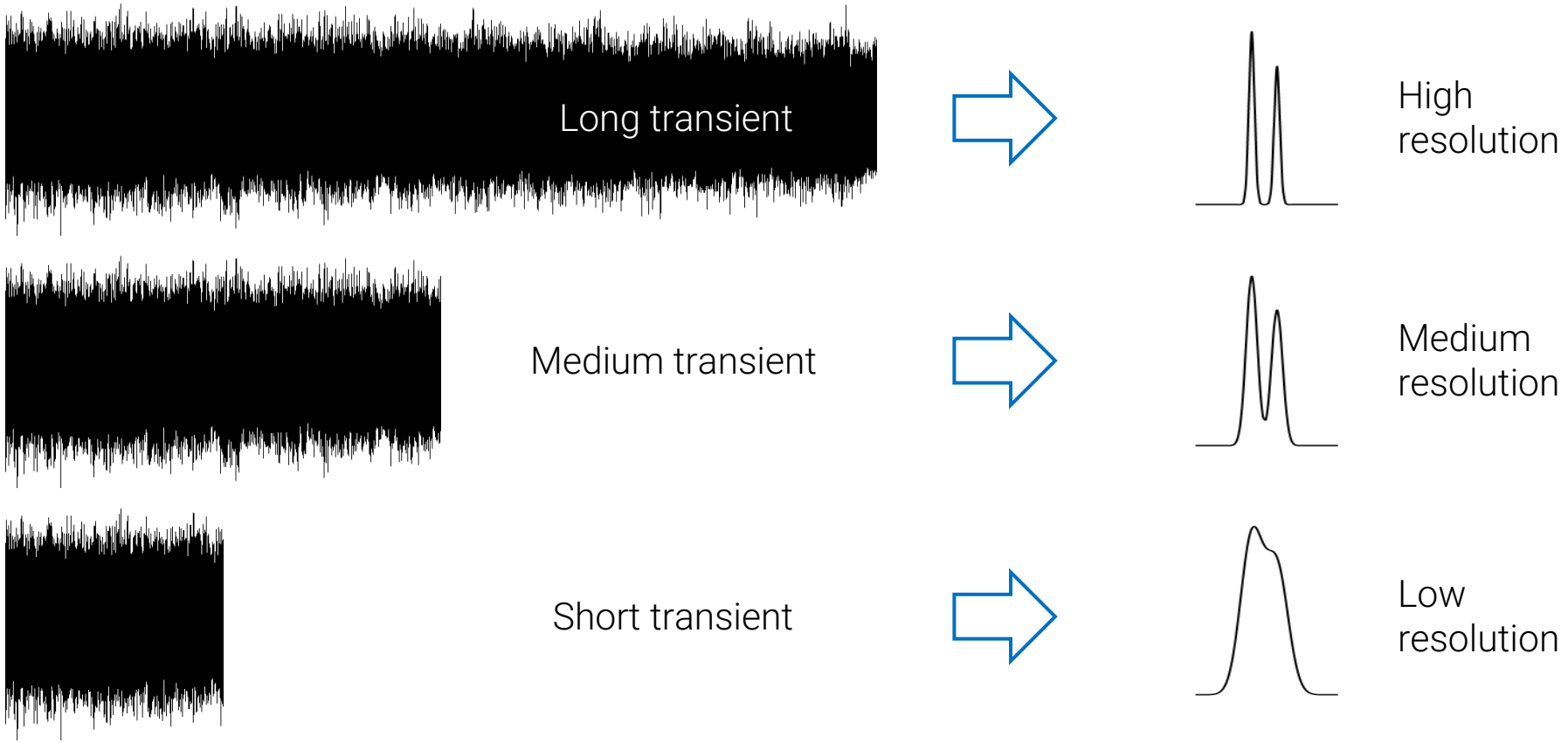


ParaCell stabilizes low abundant ions

FT



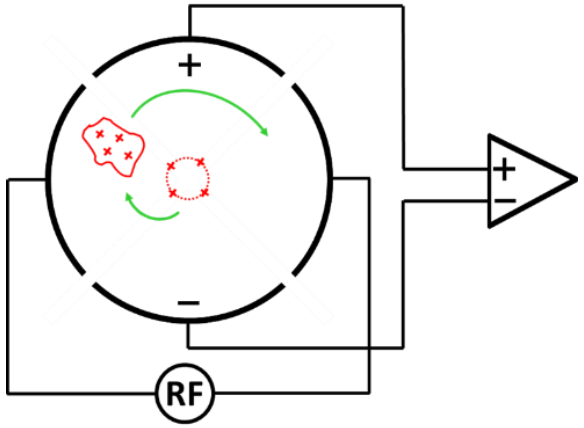
Effect of Transient Length and Resolution



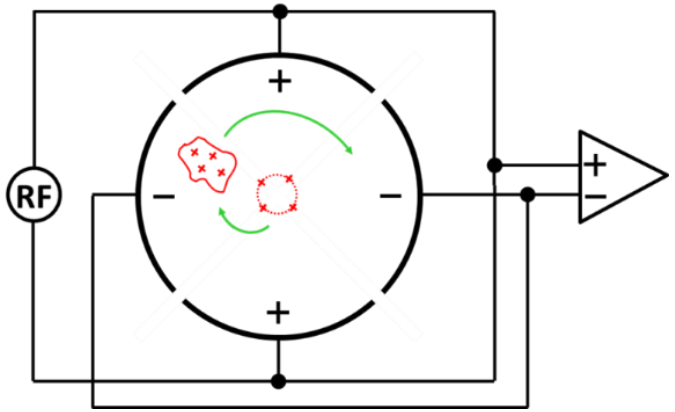
MRMS can trade resolution for speed or speed for resolution.
MRMS has no limit of mass resolution!

1ω and 2ω detection technology

Standard 1ω Dipole Detection



2ω Quadrupolar Detection (QPD)



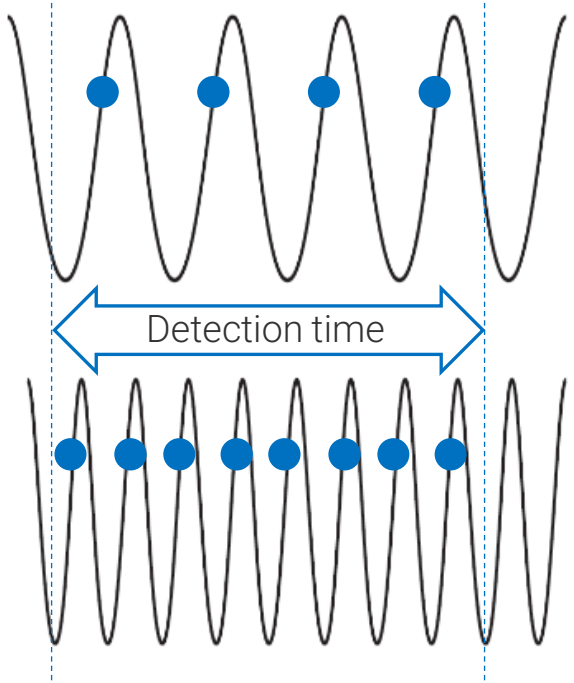
QUADRUPOLE–DETECTION FT-ICR MASS SPECTROMETRY*

L. SCHWEIKHARD, M. LINDINGER and H.-J. KLUGE

Published 1990

Direct detection of the cyclotron frequency ω_+

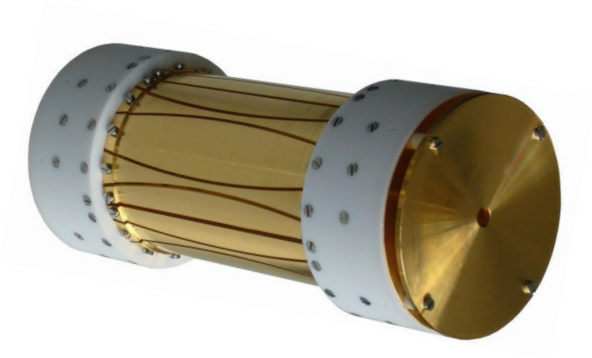
$$R_{Dipole} = \boldsymbol{\nu} \cdot \boldsymbol{T}$$



Direct detection of the **double** cyclotron frequency $2\omega_+$

$$R_{QPD} = \mathbf{2} \cdot \boldsymbol{\nu} \cdot \boldsymbol{T} = \mathbf{2} \cdot R_{Dipole}$$

xR detection



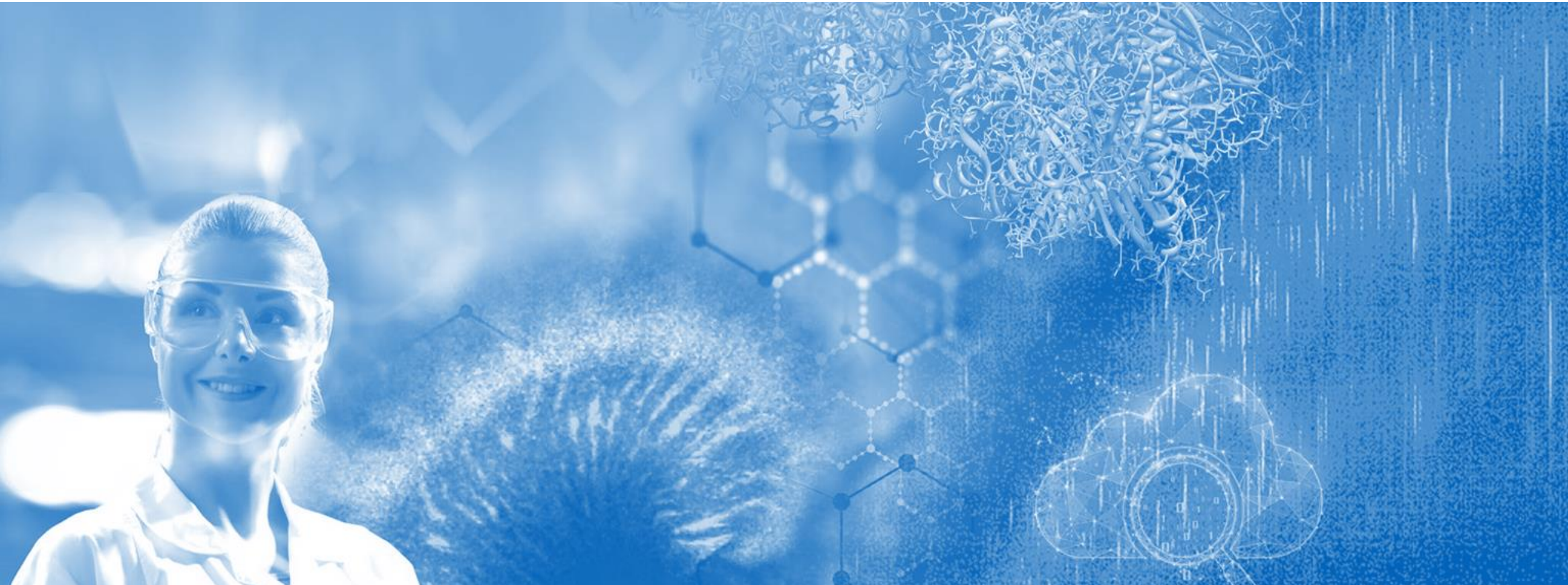
⇨ information

⇨ Doubled amount of information

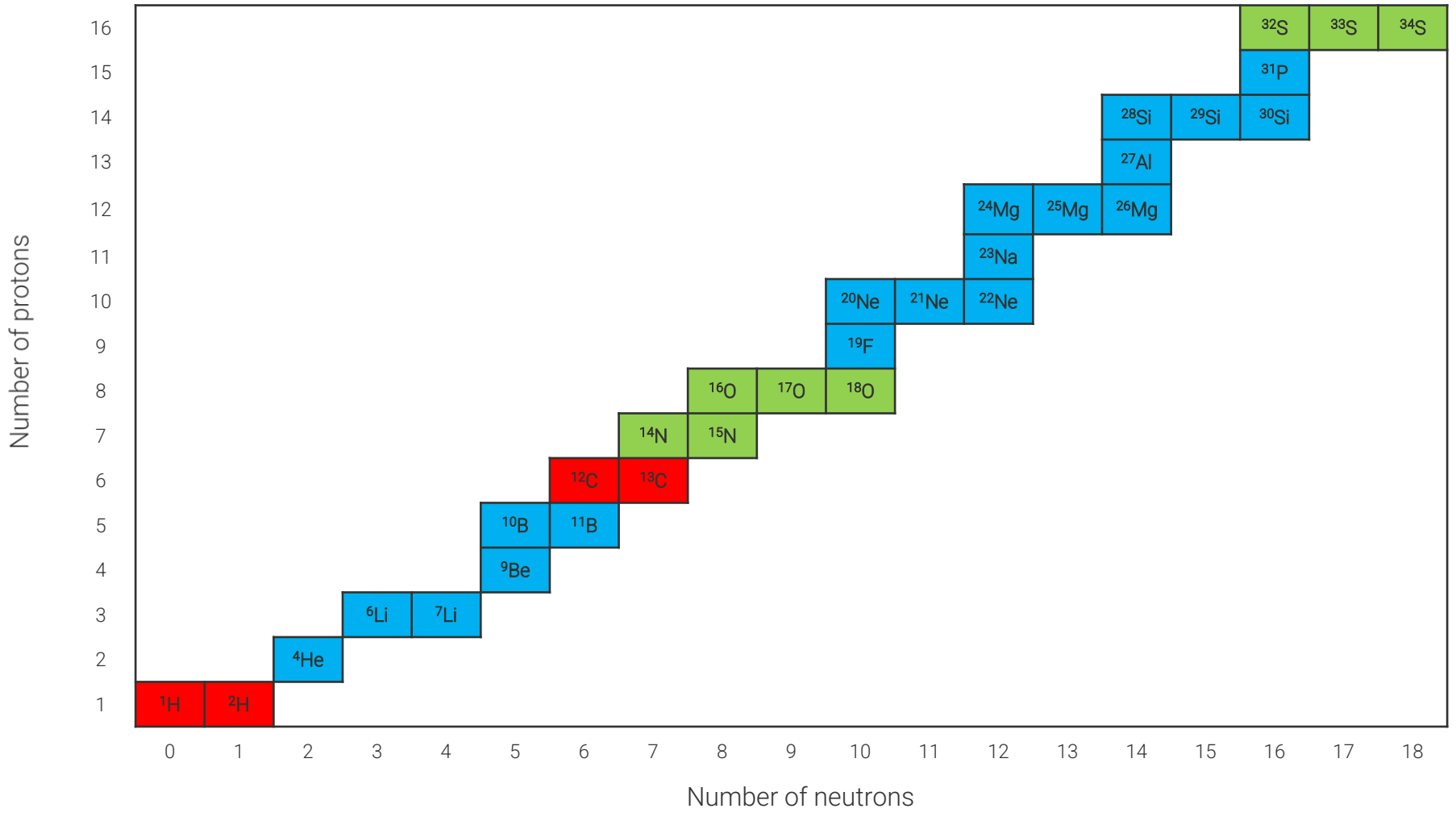
2xR

double resolution
or
double speed

Isotopes



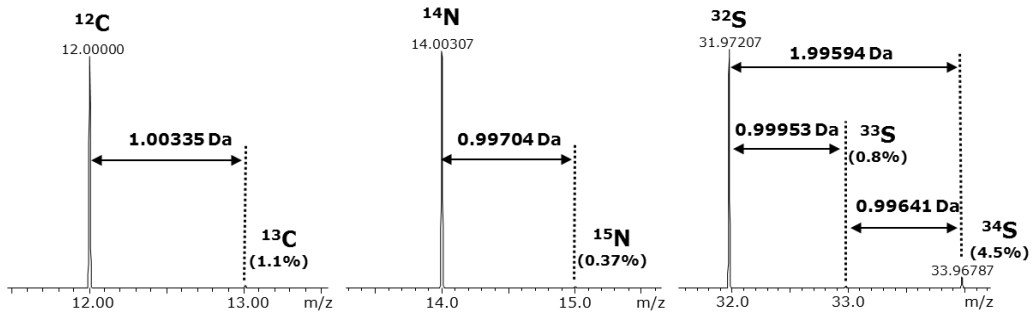
Introduction – stable isotopes



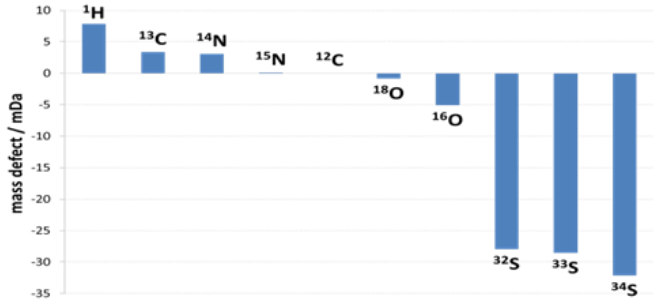
Isotopes

Nature offers a way to avoid wrong formula assignments error:

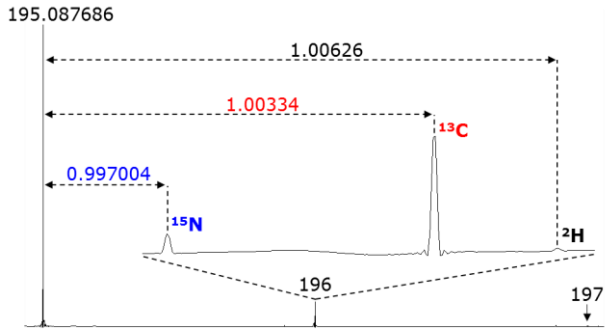
- Chemical elements consist of isotopes with different abundance. E.g. carbon consists mainly of ^{12}C with 1.1% heavier ^{13}C



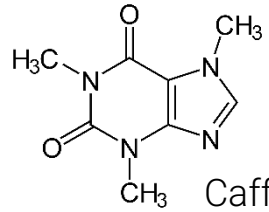
- Due to the mass defect, the mass difference between these isotopes are non integer values, e.g. $\Delta(^{12}C;^{13}C)$ = 1.00335 Da
- The mass difference between different isotopes are different



- *Example:* IFS of caffeine (measured with 7T 2xR)
- IFS yields information on the elemental composition of the analyte



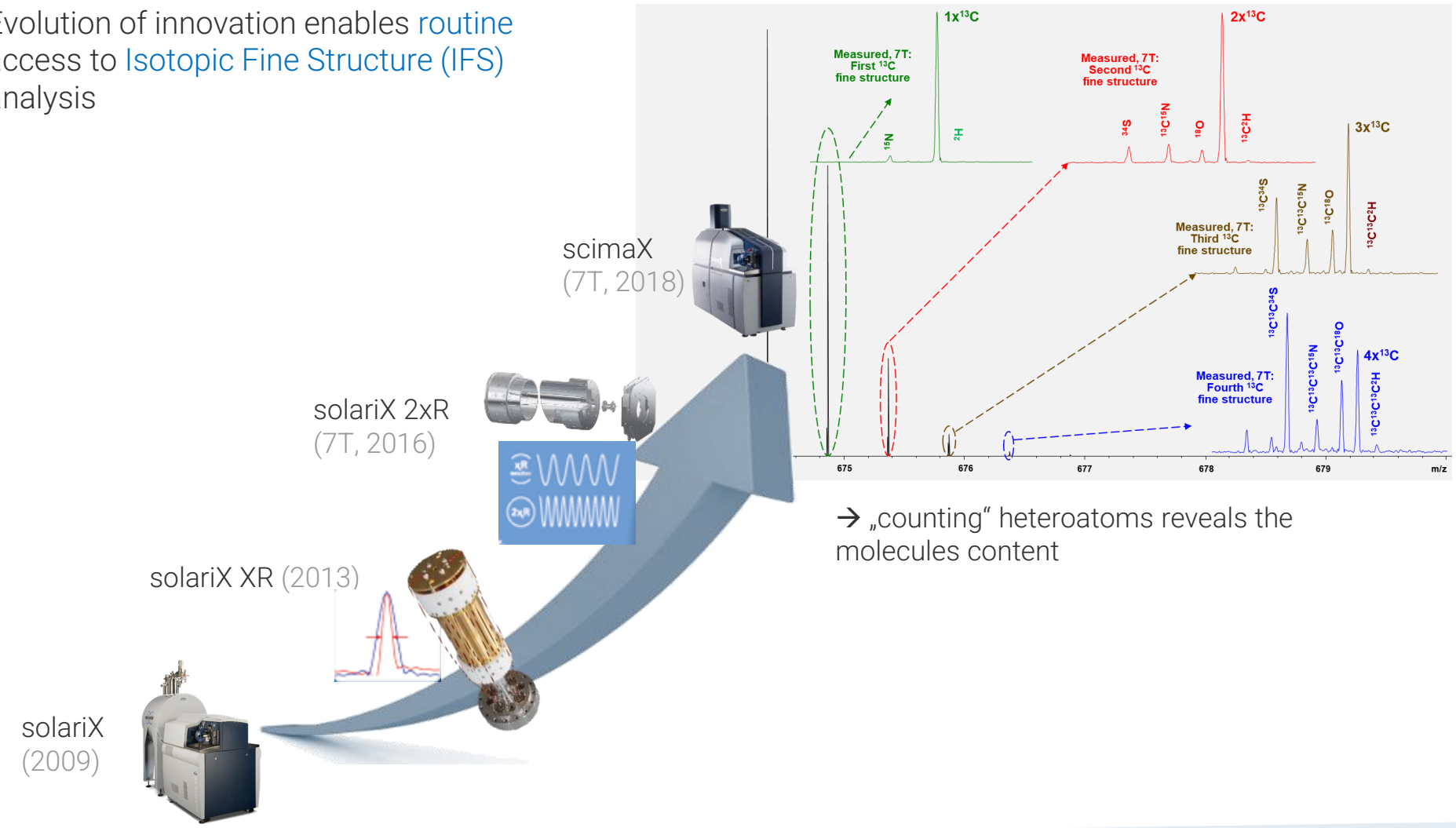
molecule contains N, C and H



Caffeine

MRMS provides Isotopic Fine Structure

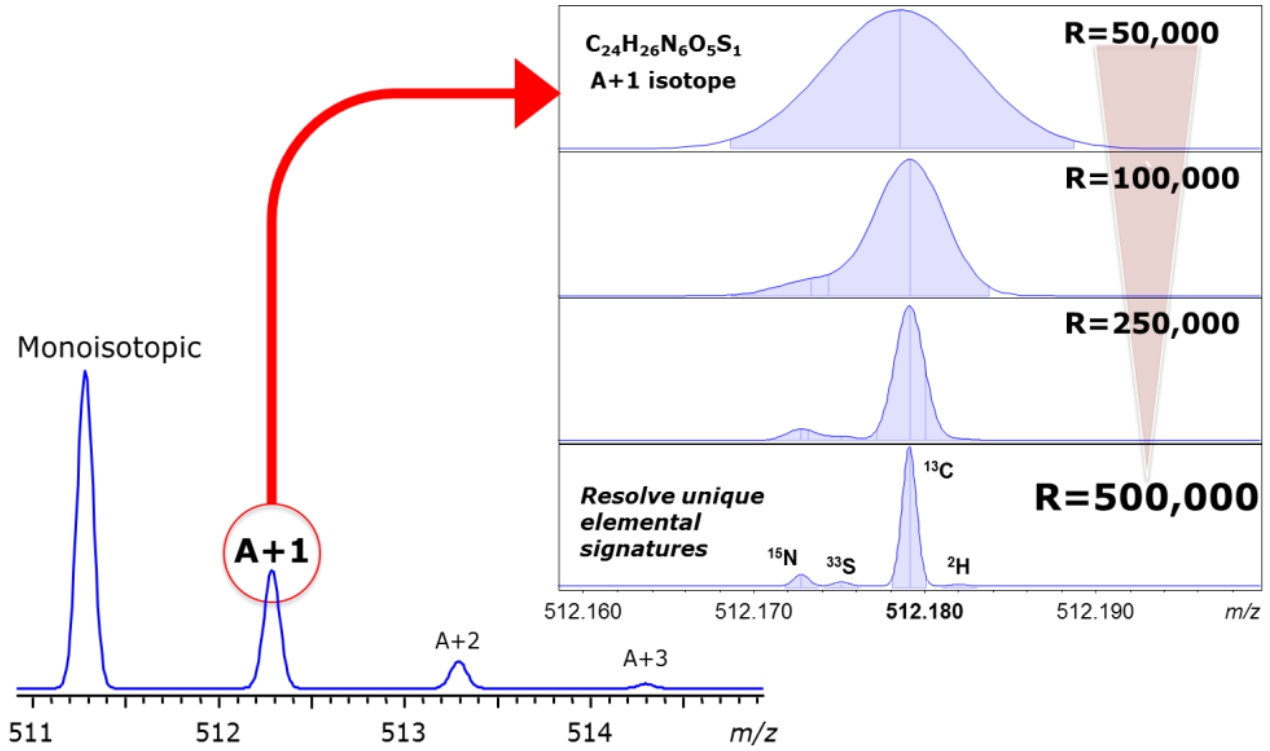
Evolution of innovation enables routine access to Isotopic Fine Structure (IFS) analysis



→ „counting“ heteroatoms reveals the molecules content

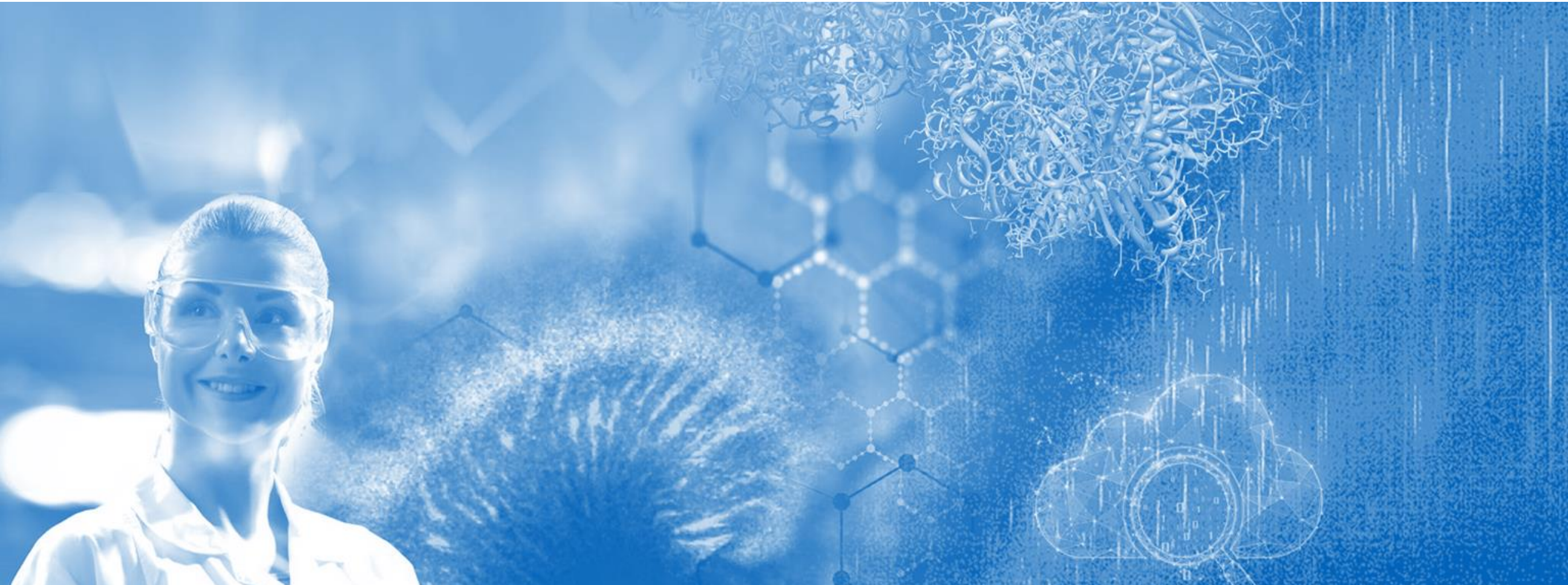
Isotopic Fine Structure

eXtreme Resolution enables confident results



Example: A+1 peak of $C_{24}H_{26}N_6O_5S_1$

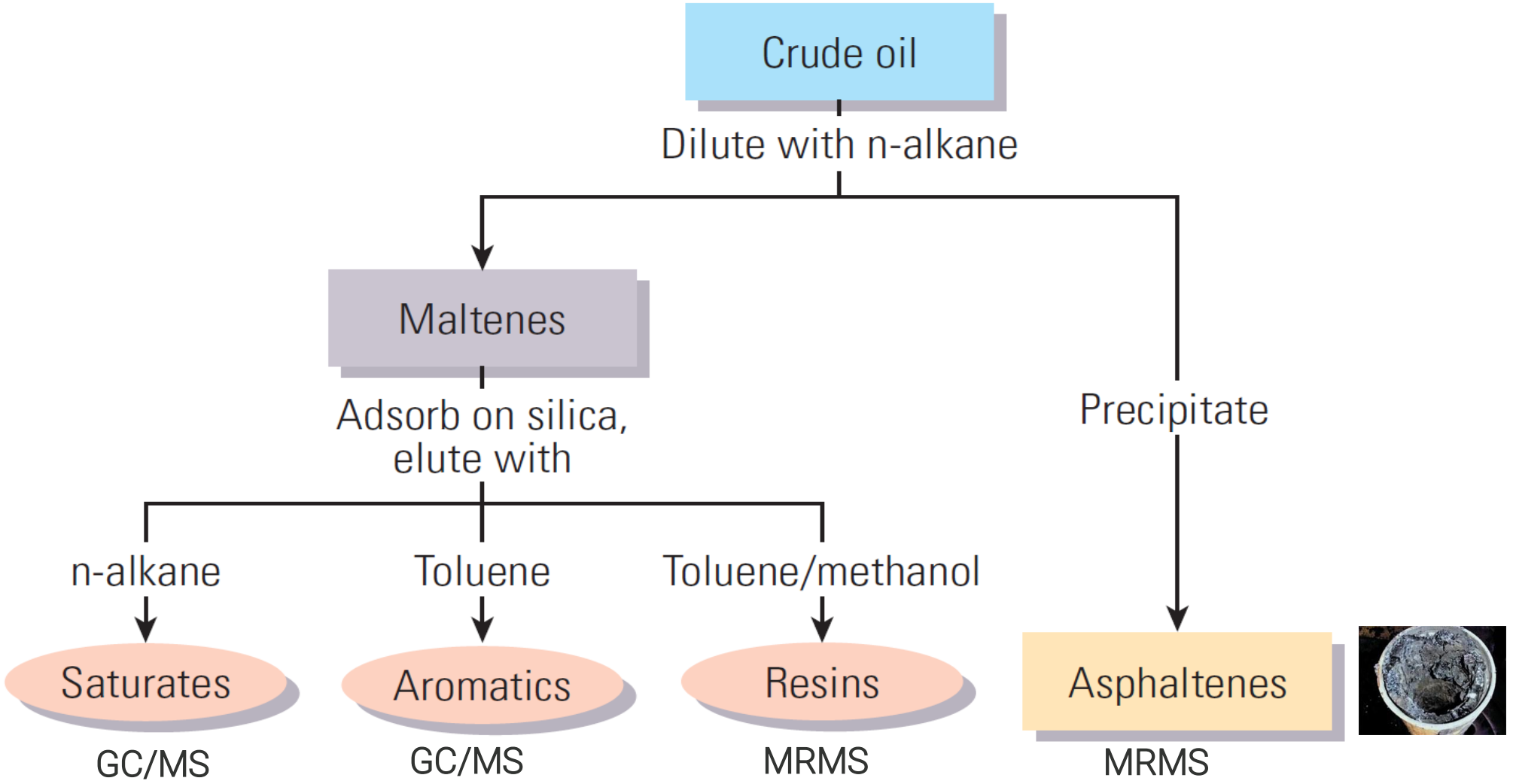
Application of ultra-high mass resolution: Complex mixtures - petroleomics



Introduction to petroleomics

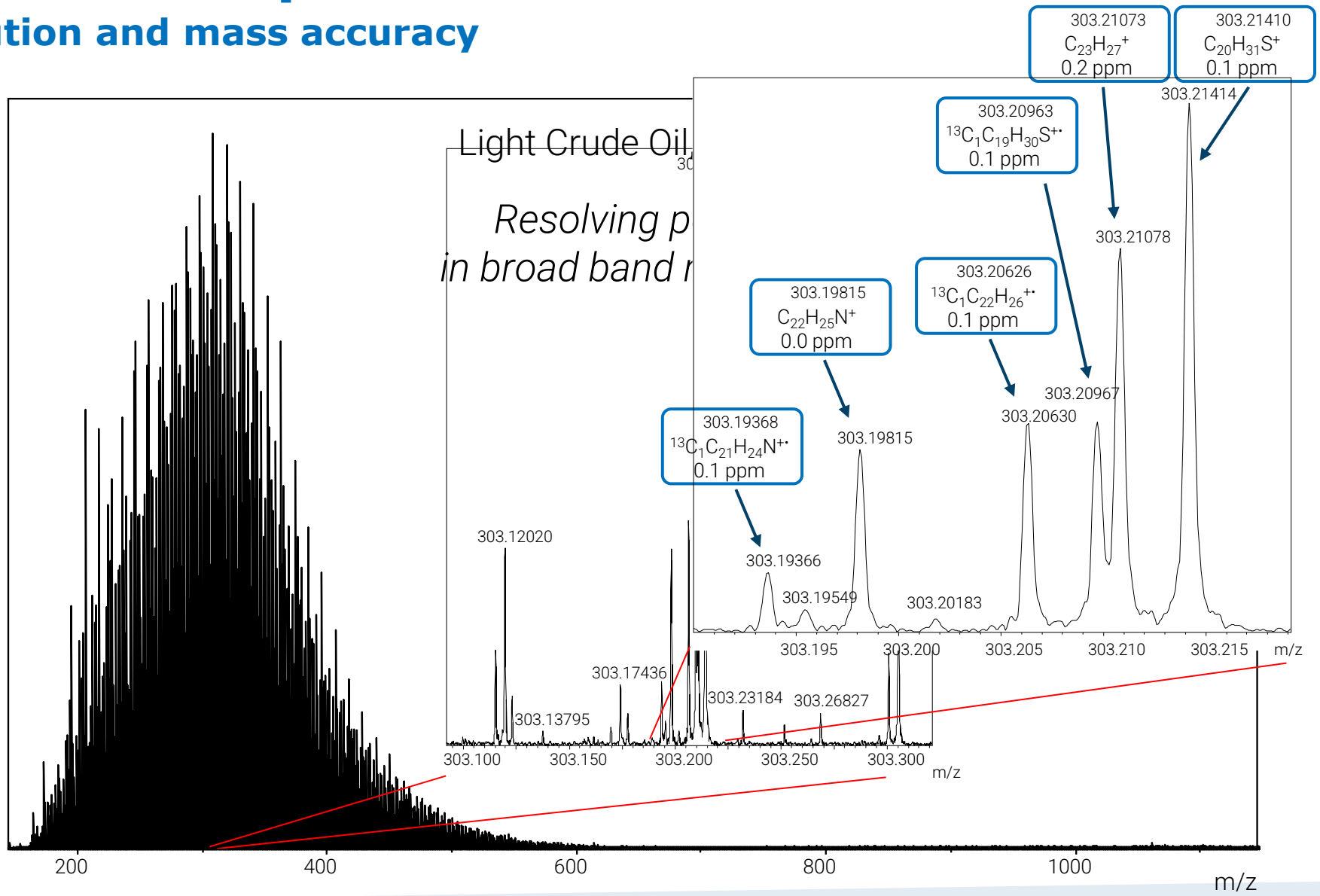
SARA Fractionation

K. Akbarzadeh et al., Oilfield Review, Asphaltenes - Problematic but Rich in Potential, 2007.



Mass spectra in petroleomics

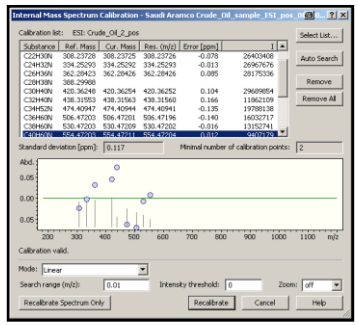
Mass resolution and mass accuracy



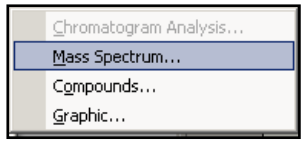
Data processing in petroleomics

Data processing

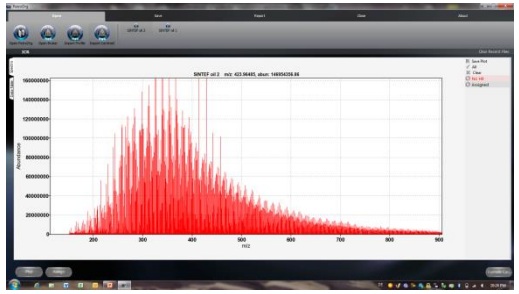
Internal recalibration



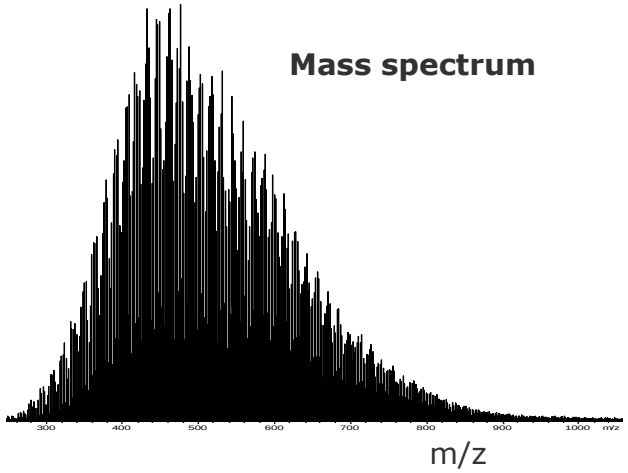
Export mass spectrum



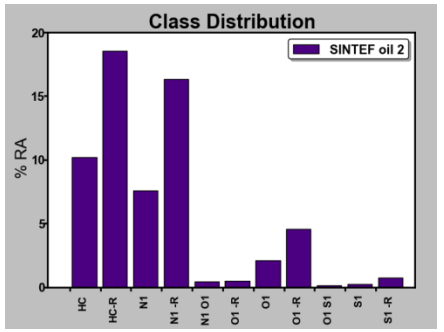
PetroOrg software
Molecular Formula calculation



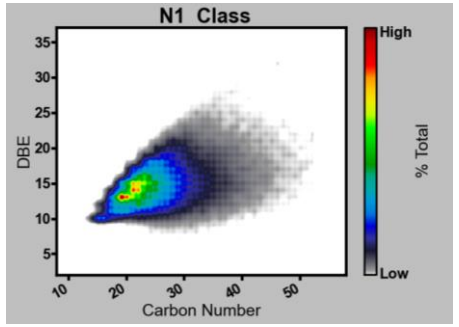
Mass spectrum



Class distribution plot



DBE vs. C plot

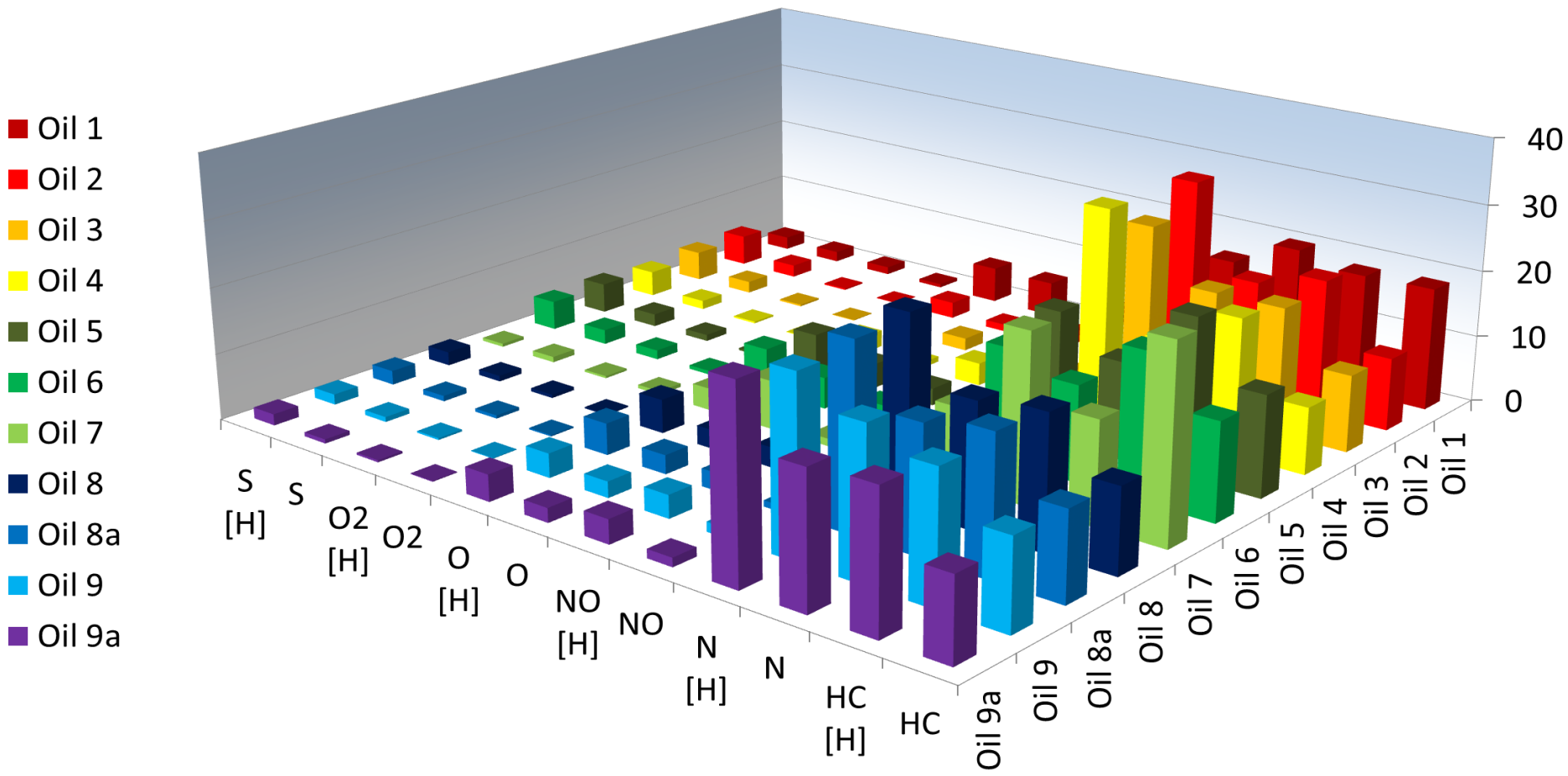


Compound classes of crude oils

Variation of crude oils

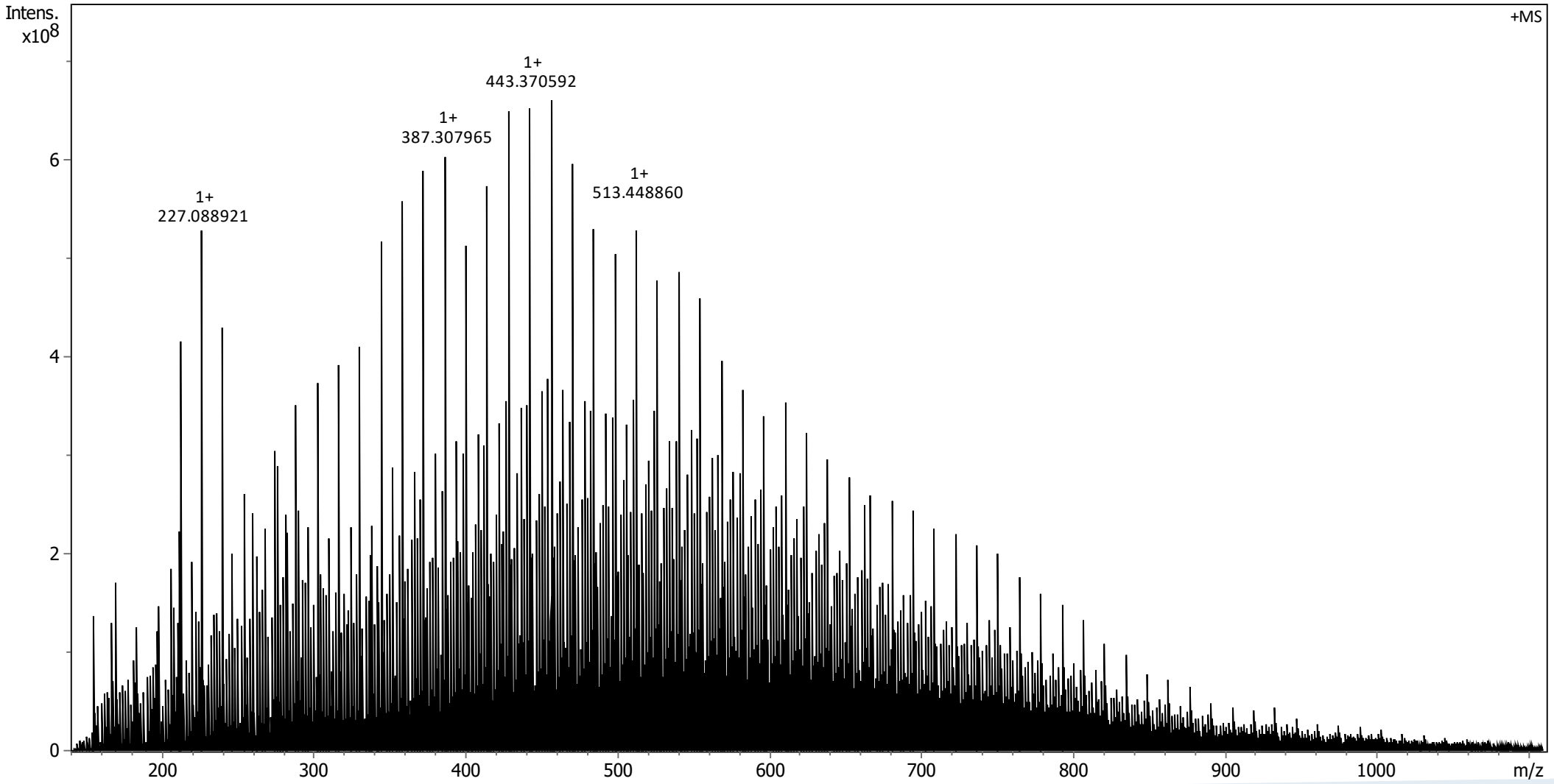
Oil 8 and 8a: identical oils from different bottles
Oil 9a: Oil 9 one day in ion source at 3 mbar

*Samples have been kindly provided by Dr. Kolbjørn (SINTEF, Trondheim, Norway)



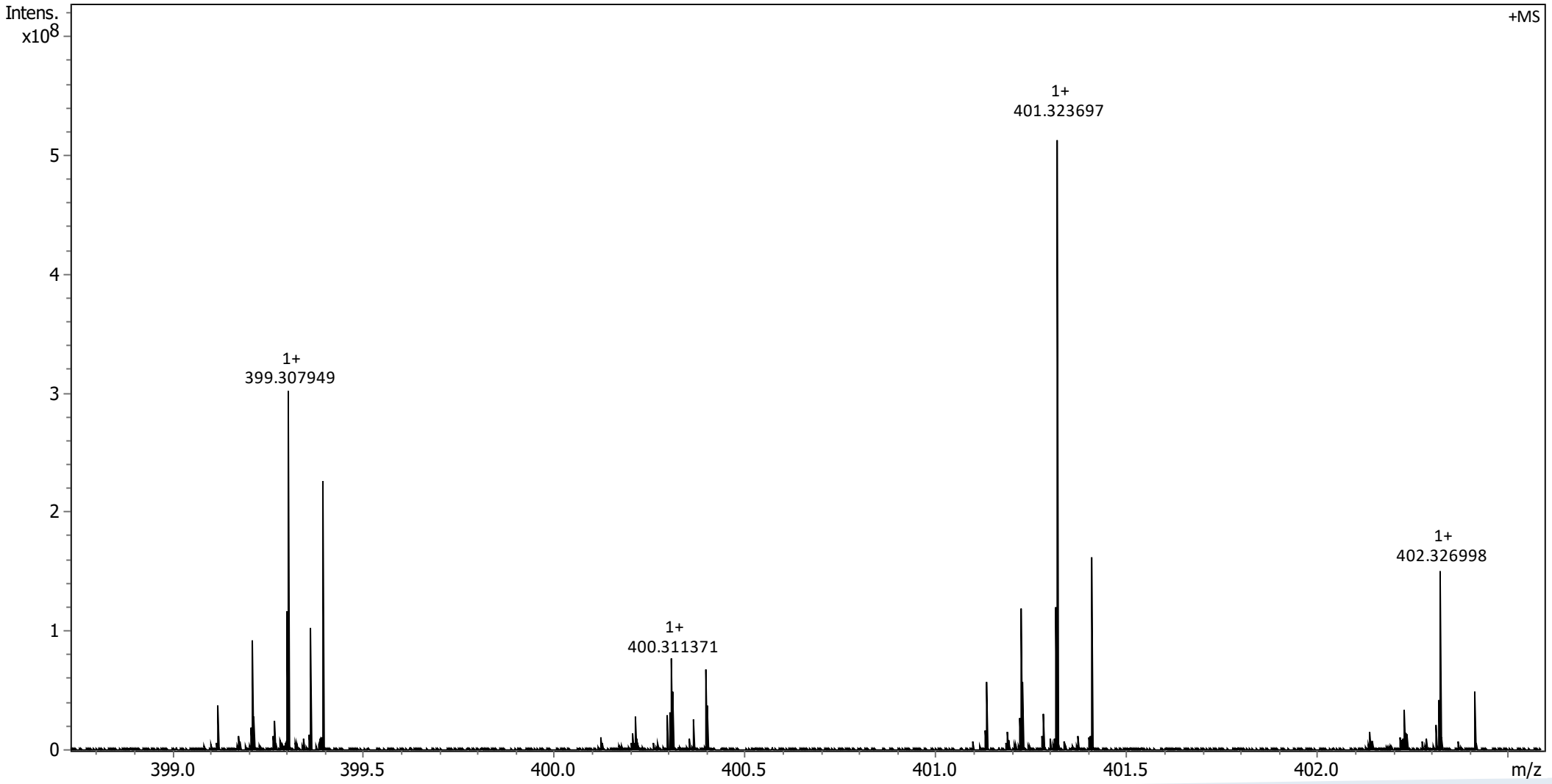
Measurement of a complex asphaltene

APCI results - Overview of spectra



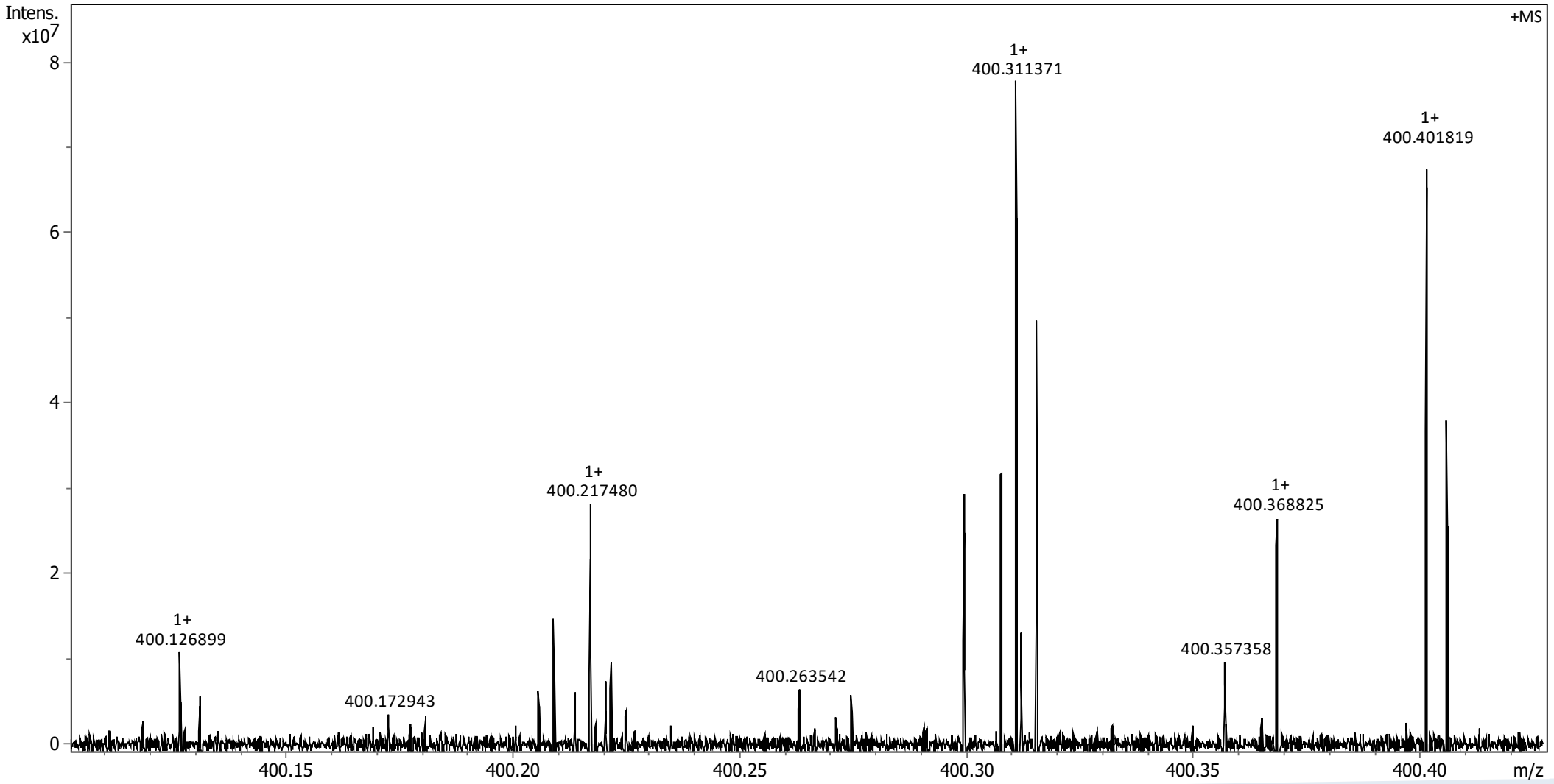
Measurement of a complex asphaltene

APCI results - Zoom in @ m/z 399 - 403



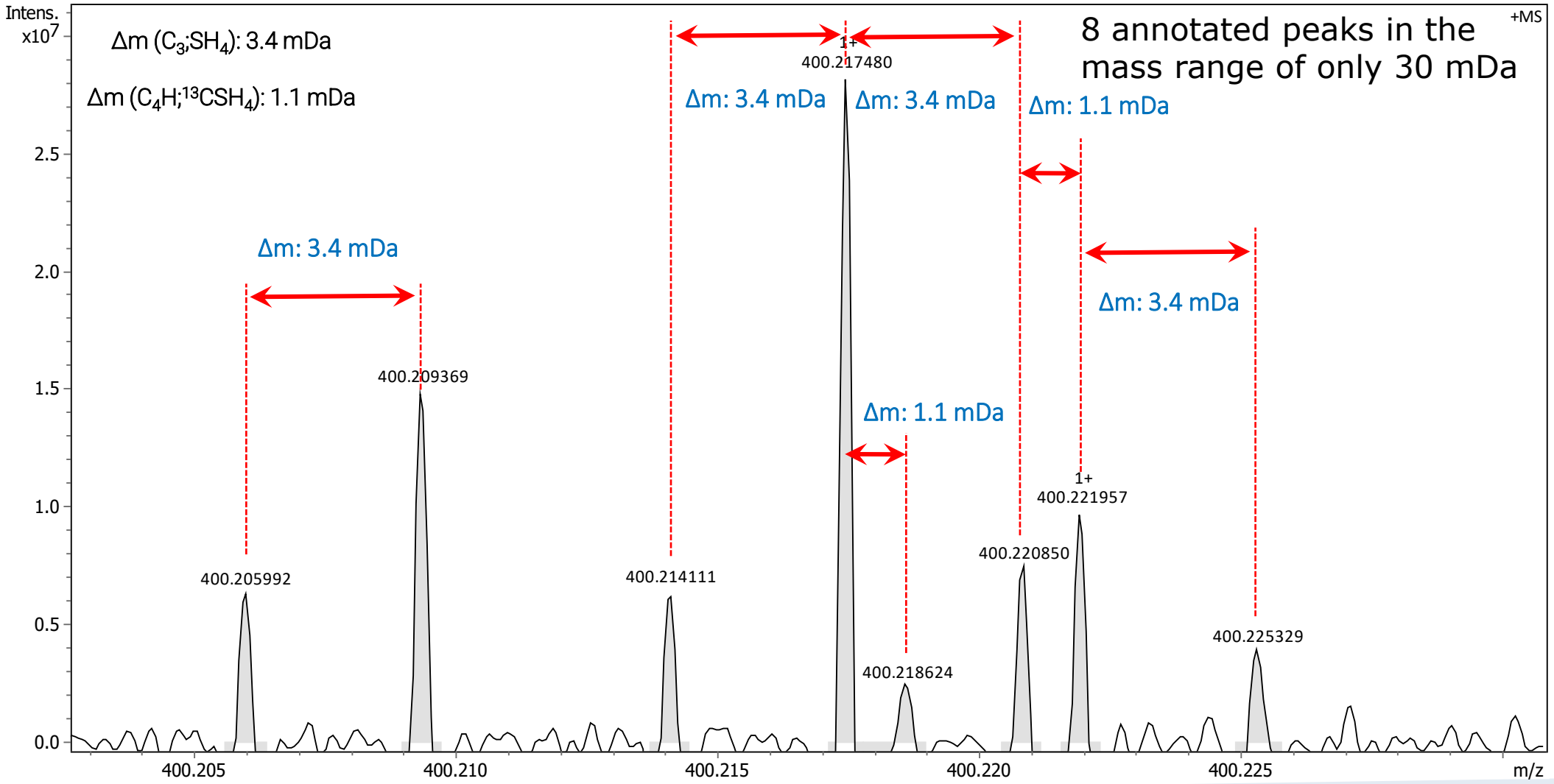
Measurement of a complex asphaltene

APCI results - Zoom in @ m/z 400



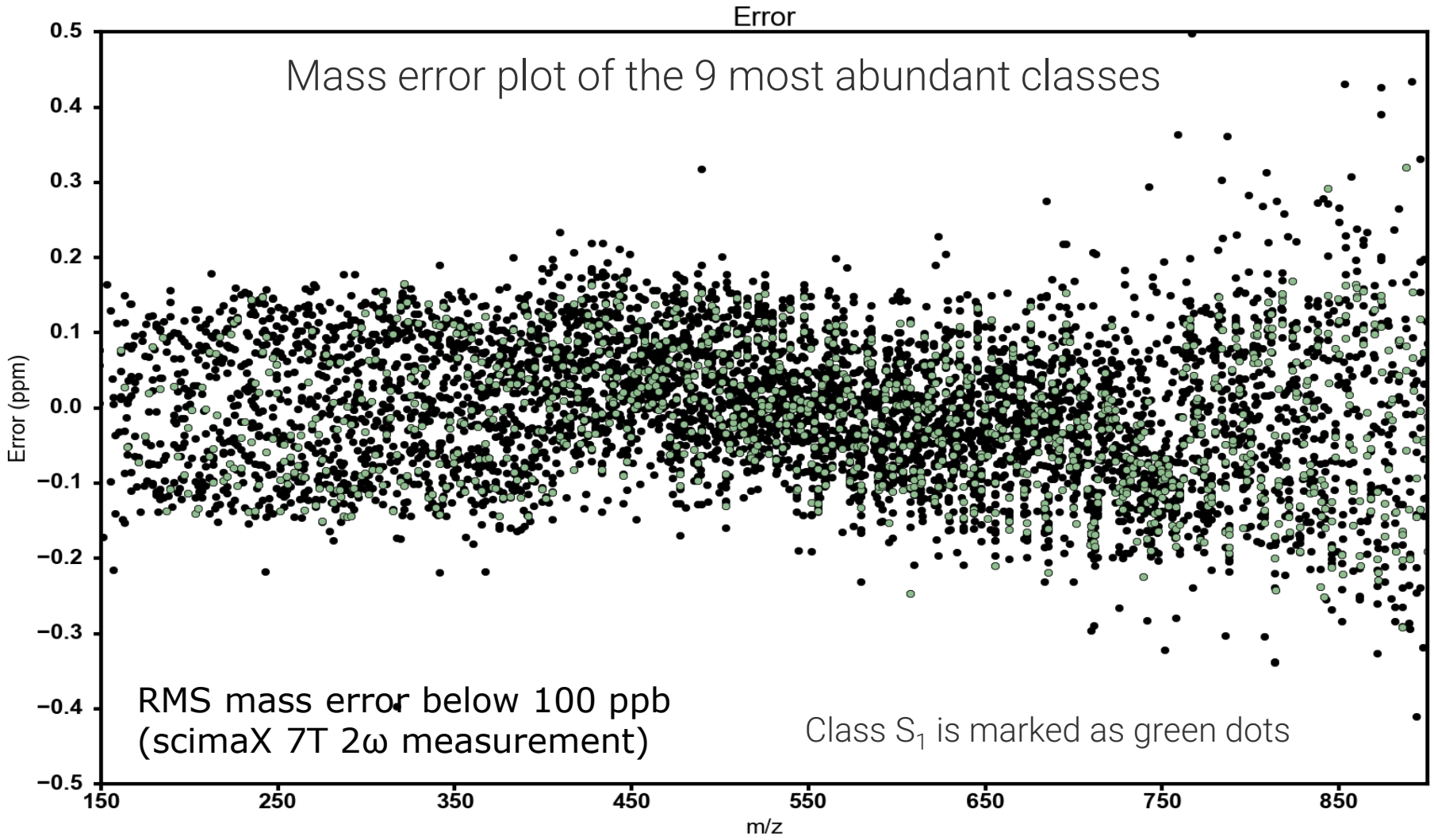
Measurement of a complex asphaltene

APCI results - Zoom in @ m/z 400.20 – 400.23



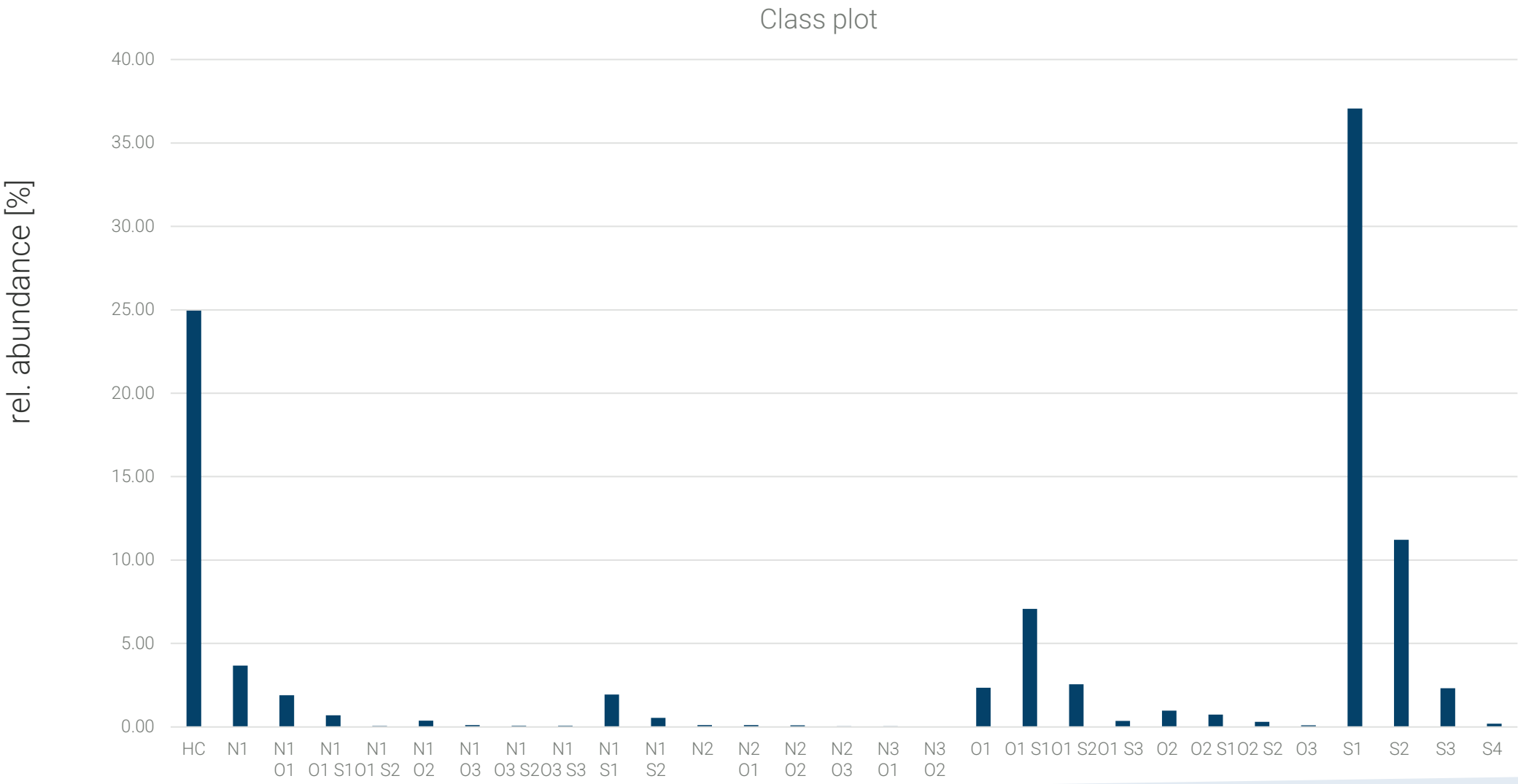
Measurement of a complex asphaltene

APCI results - Mass error plot



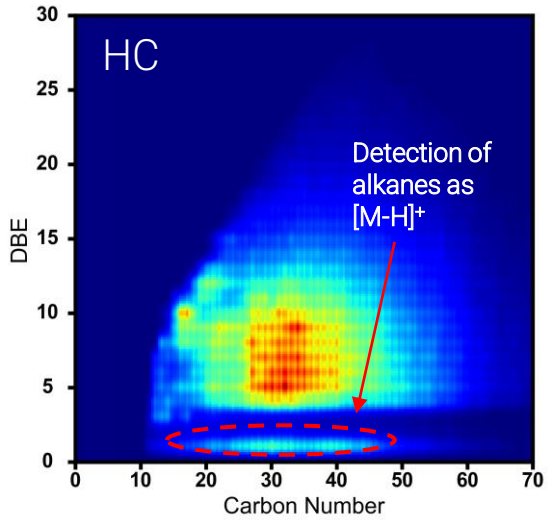
Measurement of a complex asphaltene

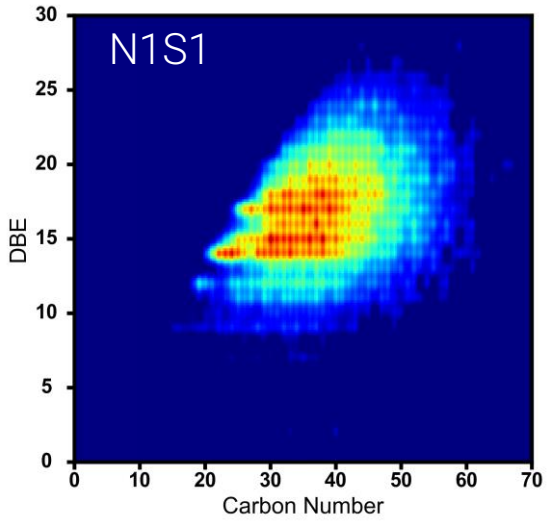
APCI results - Class plot

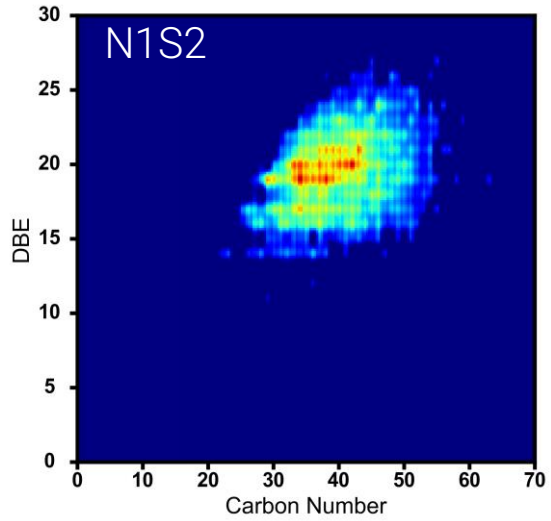


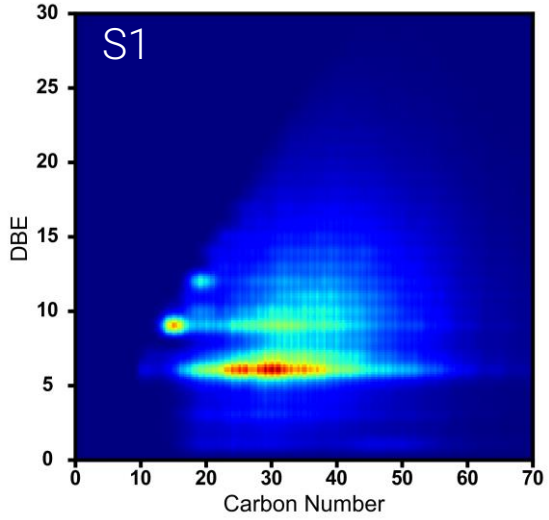
Measurement of a complex asphaltene

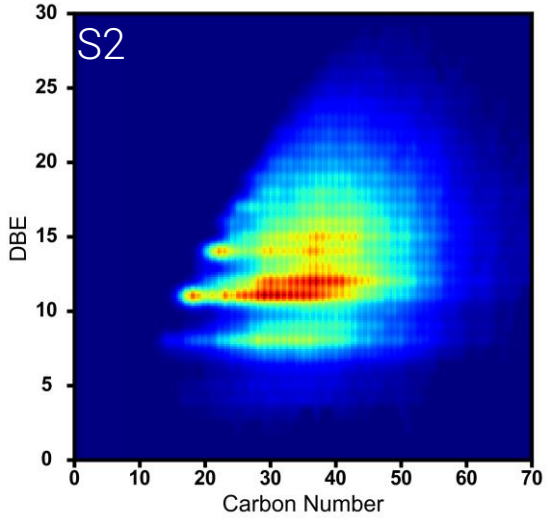
APCI results - DBE vs. C plots of different classes

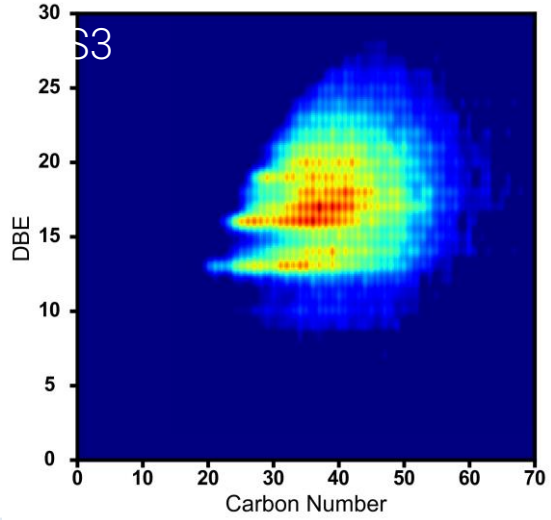








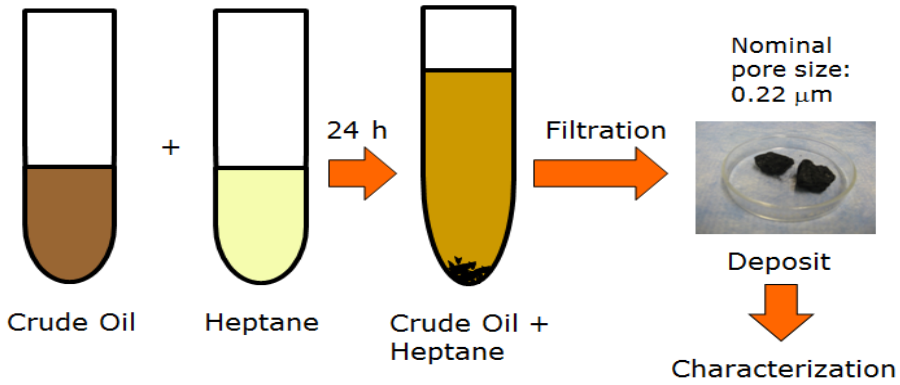


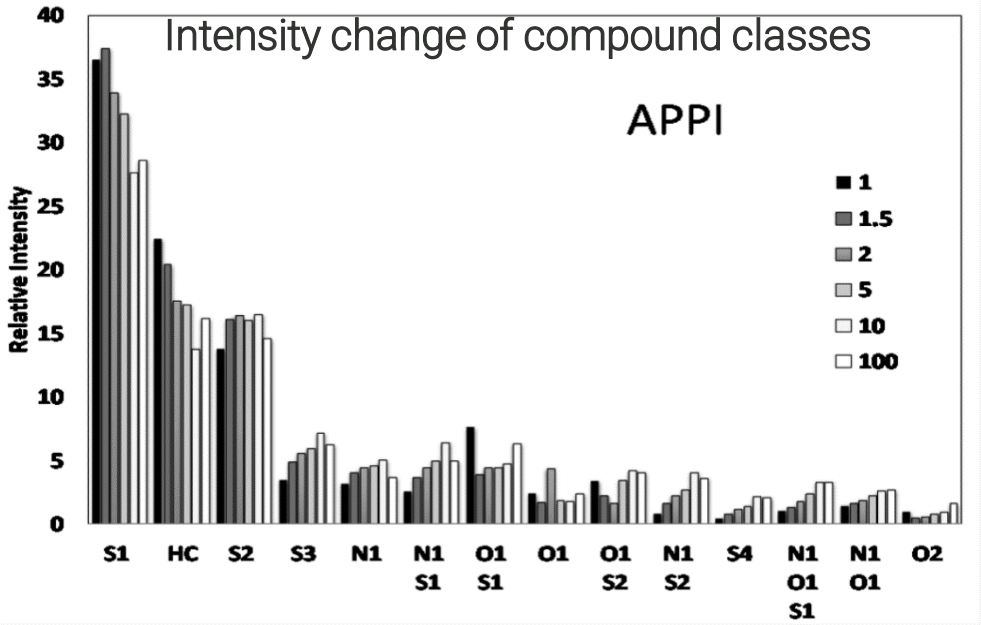


Asphaltene fractions

Precipitated at asphaltenes at different solvent power

E. Rogel, M. Witt, *Energy & Fuels* 2018, 32, 2653-2660.





HCOR	C (wt %)	H (wt %)	H/C molar ratio
1	82.86	11.01	1.59
1.5	83.58	10.41	1.49
2	84.08	10.00	1.43
5	80.94	8.72	1.29
10	81.35	8.41	1.24
100	80.33	8.04	1.20

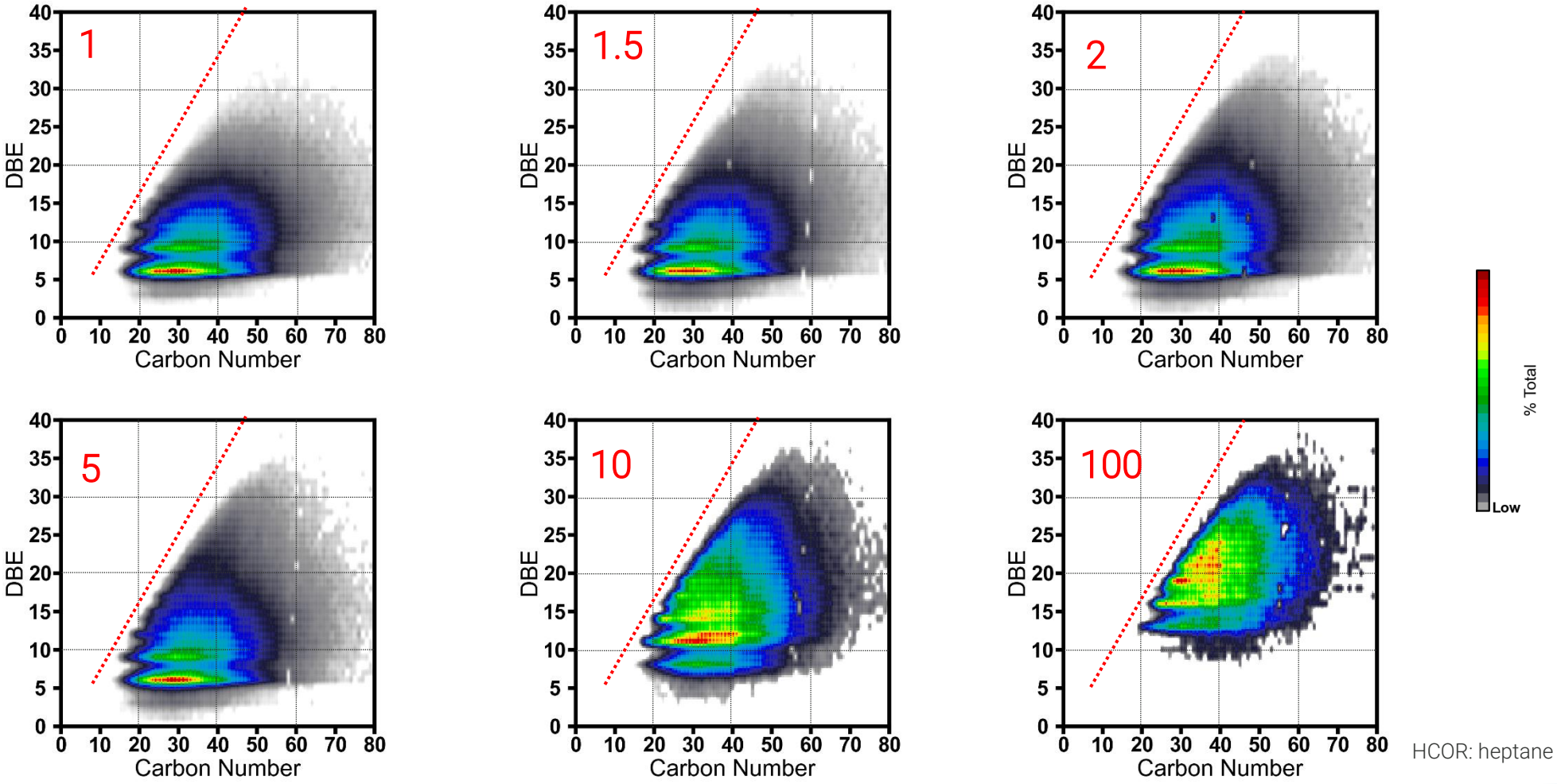
HCOR: heptane crude oil ratio

Asphaltene fractions

Precipitated at asphaltenes at different solvent power

E. Rogel, M. Witt, *Energy & Fuels* 2018, 32, 2653-2660.

Distribution shifts with higher HCOR to higher DBE

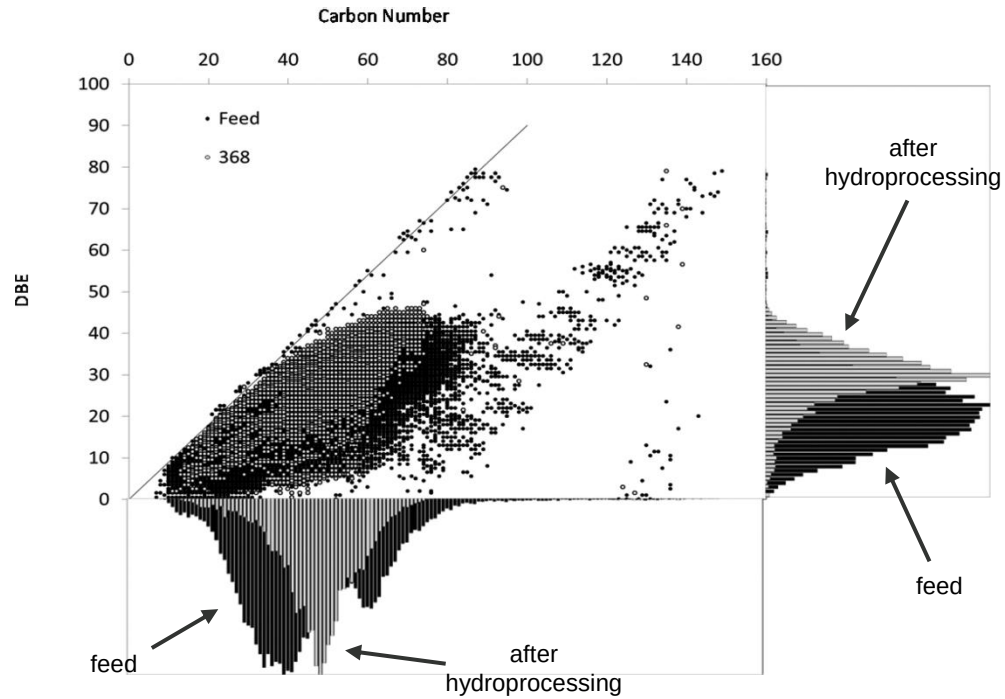


HCOR: heptane crude oil ratio

Crude oil

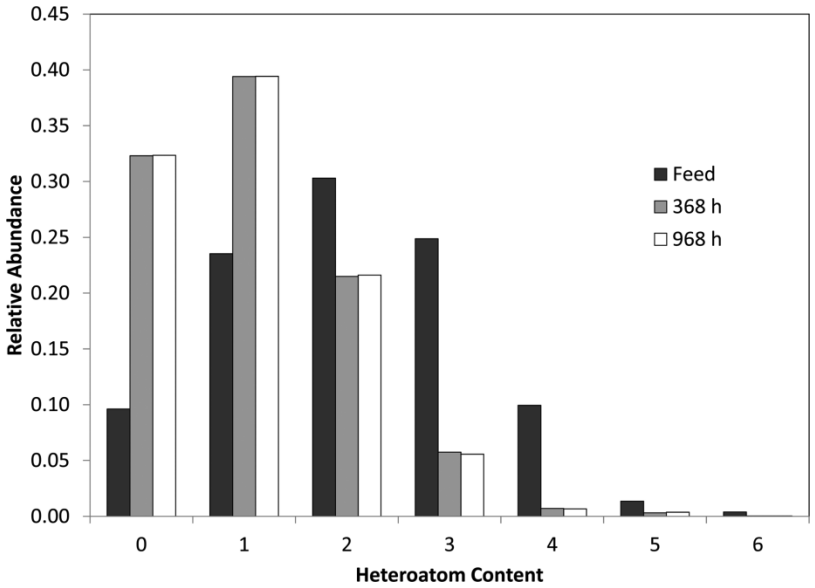
Hydroprocessing

E. Rogel, M. Witt, *Energy & Fuels* 2017, 31, 3409-3416.



Comparison of the compositional space occupied by molecules that disappeared from the feed during processing to those that appeared in the products.

Heteroatom contents as a function of time on stream

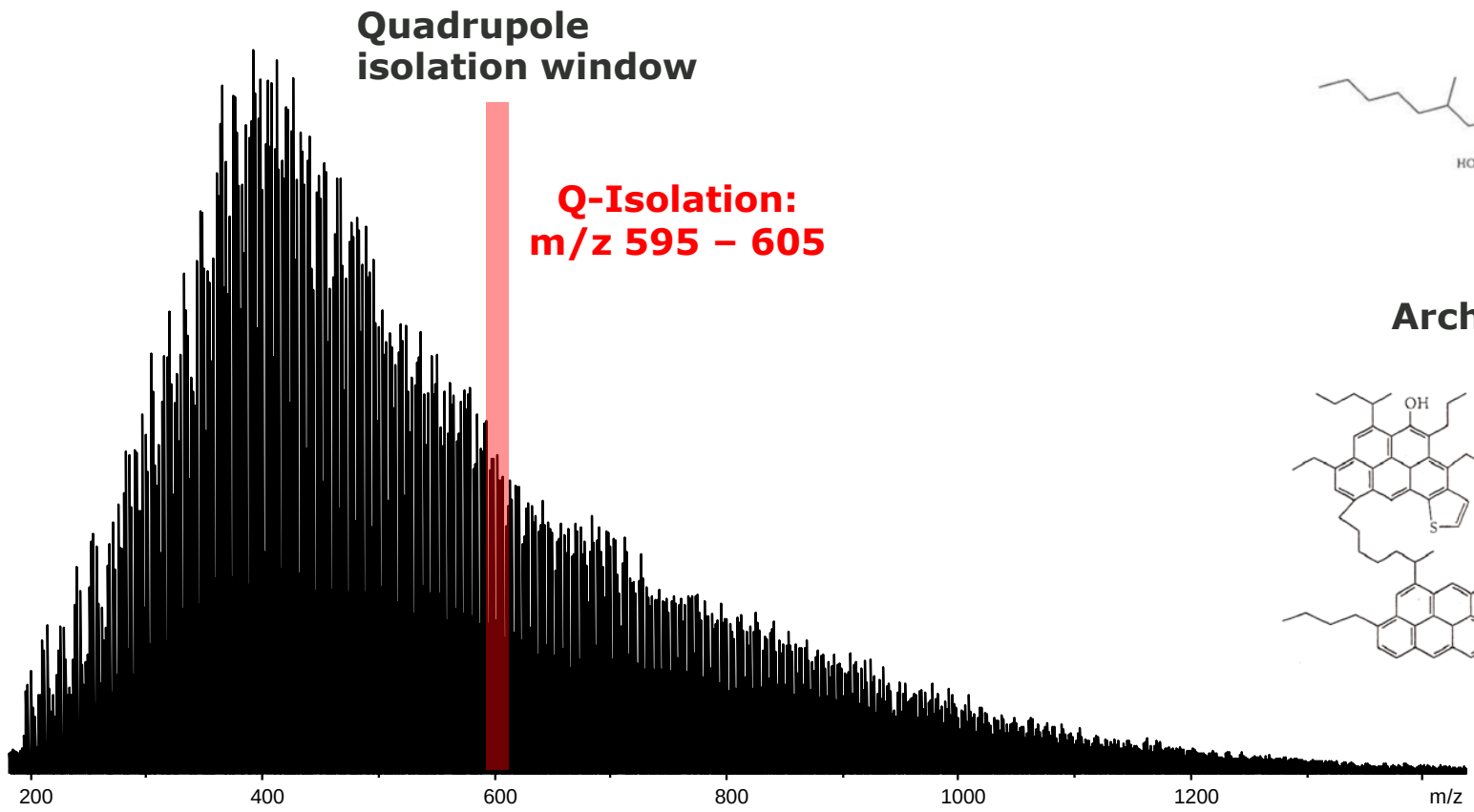


Structure of Asphaltene molecules

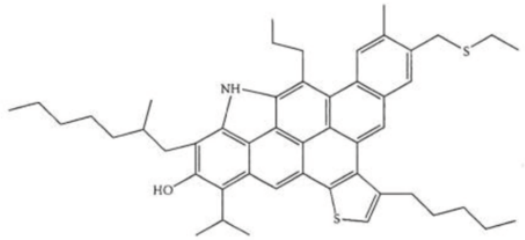
CID of an Asphaltene fractions (APPI pos)

M. Witt et al., Petrophase 2018.

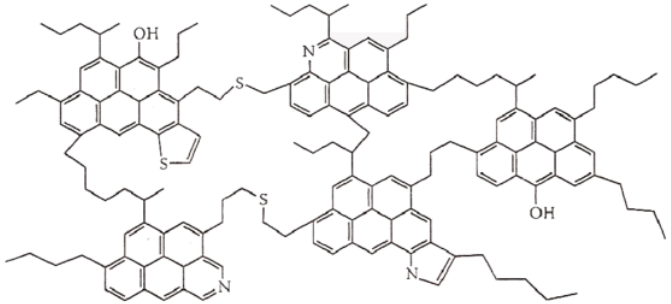
Q-isolation with a small mass window of **10 Da**.



Island structurec



Archipelago structure

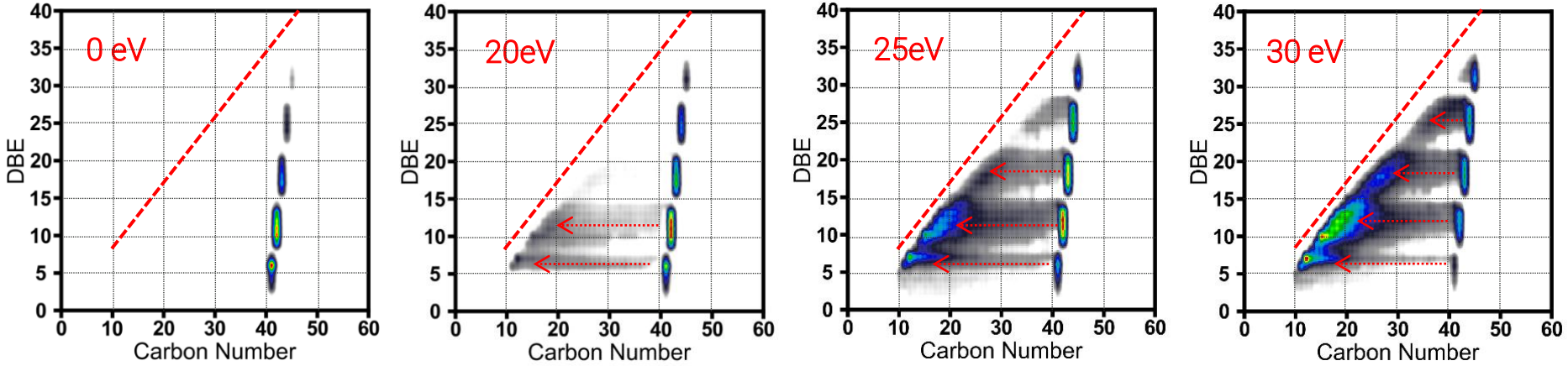


Structure of Asphaltene molecules

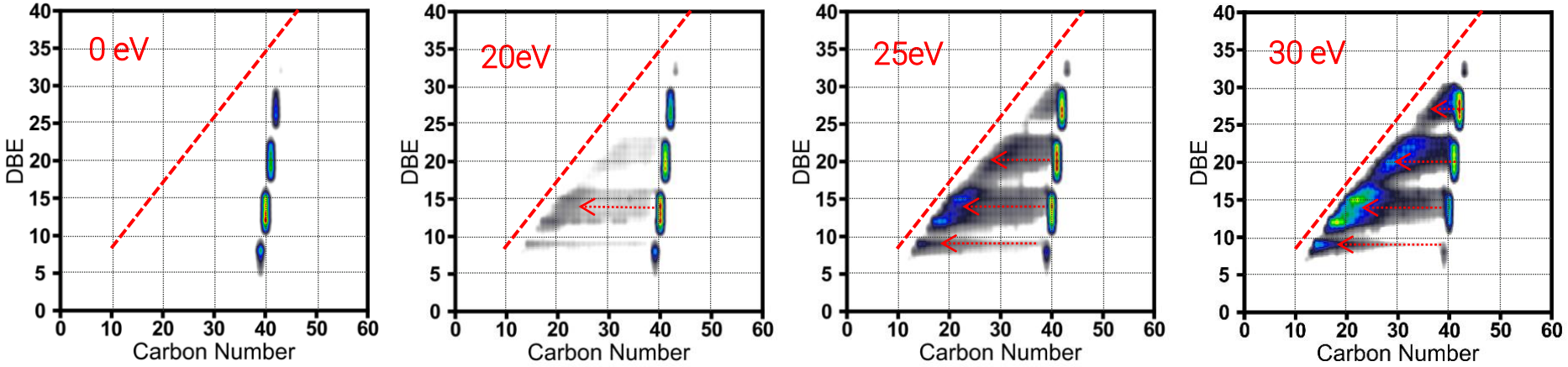
CID of an Asphaltene fractions (APPI pos)

M. Witt et al., Petrophase 2018.

Class S_1



Class S_2

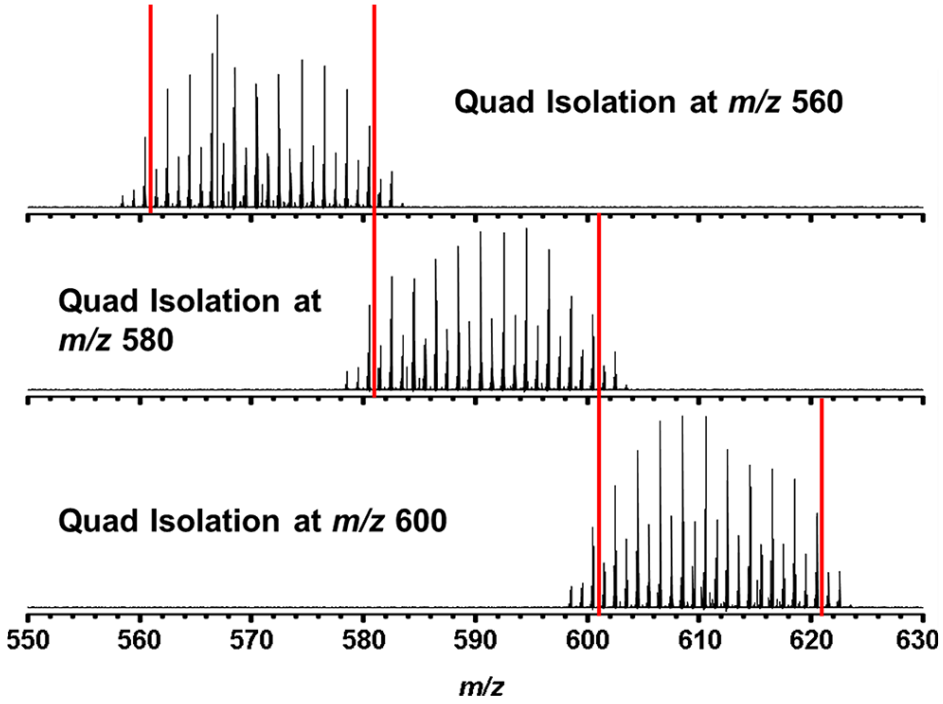


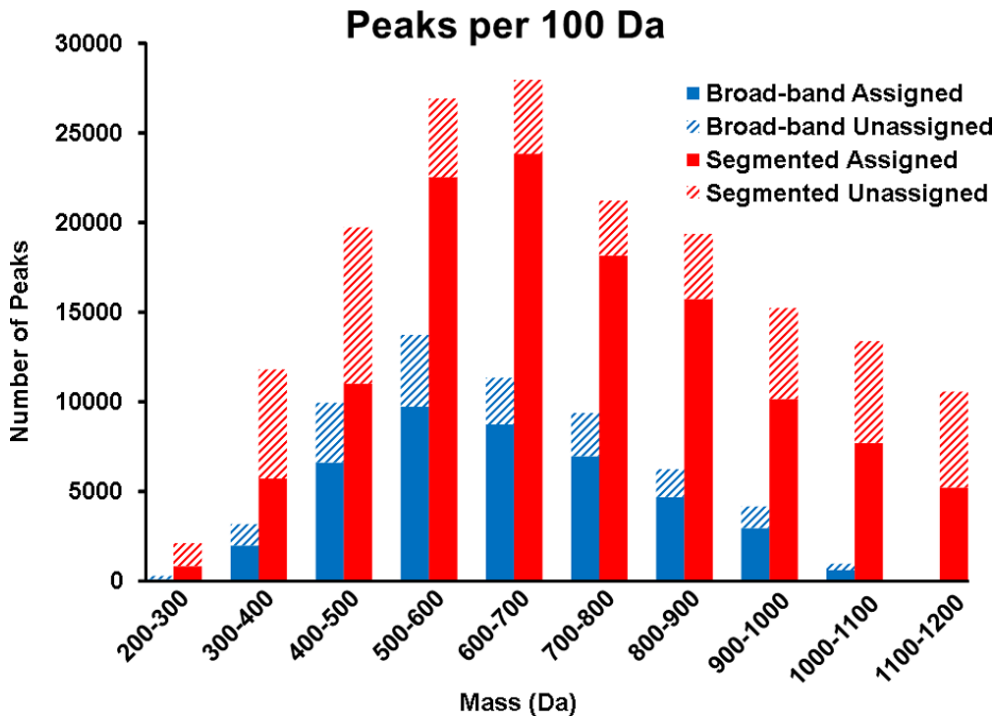
No loss is DBE ⇨ mainly island structures

Improving S/N and mass resolution

Spectra stitching

L. C. Krajewski, Anal. Chem. 2017, 89, 21, 11318–11324.

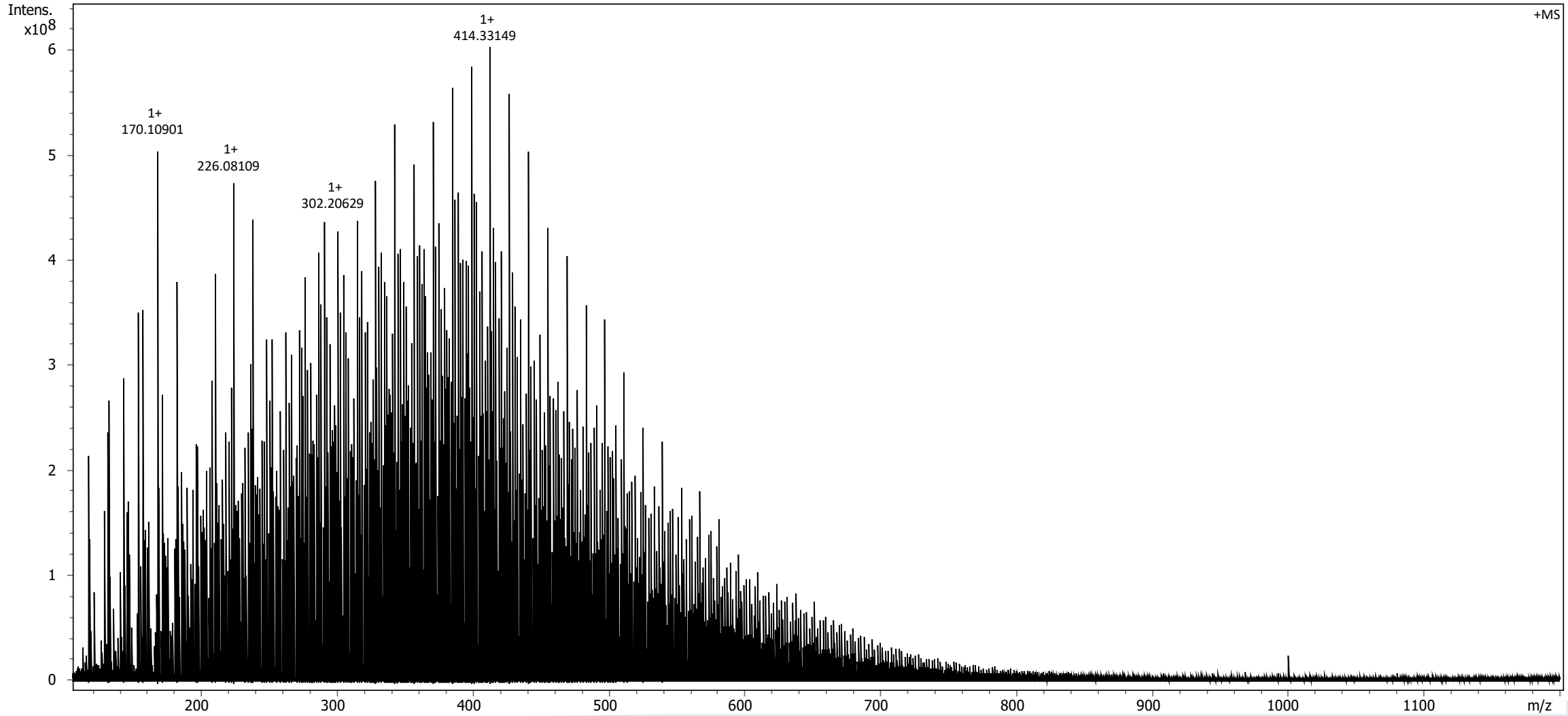




	broad band	segmented
no. of peaks	59 015	170 115
no. of assigned peaks/percentage of total	42 182 (71.5%)	126 264 (74.2%)
no. of monoisotopic peaks	23 946	67 237
rms mass error for assigned peaks (ppm)	0.19	0.13
number-average neutral mass (Da)	647.5	750.2
number-average carbon number	44.7	49.7
number-average neutral DBE	15.9	15.3
approximate total analysis time (s)	2000	37 500

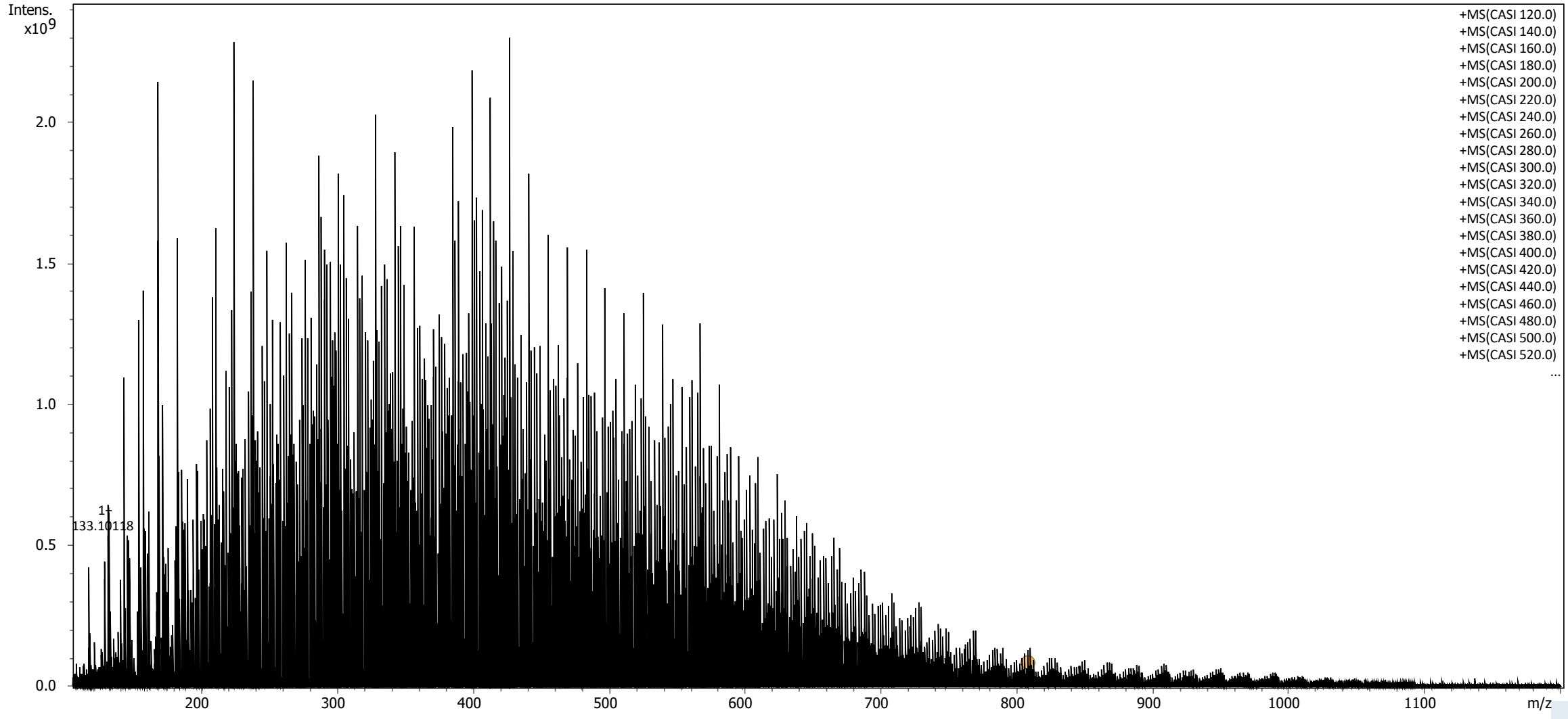
Crude oil spectrum

Broad band spectrum (APPI pos) – North sea crude oil



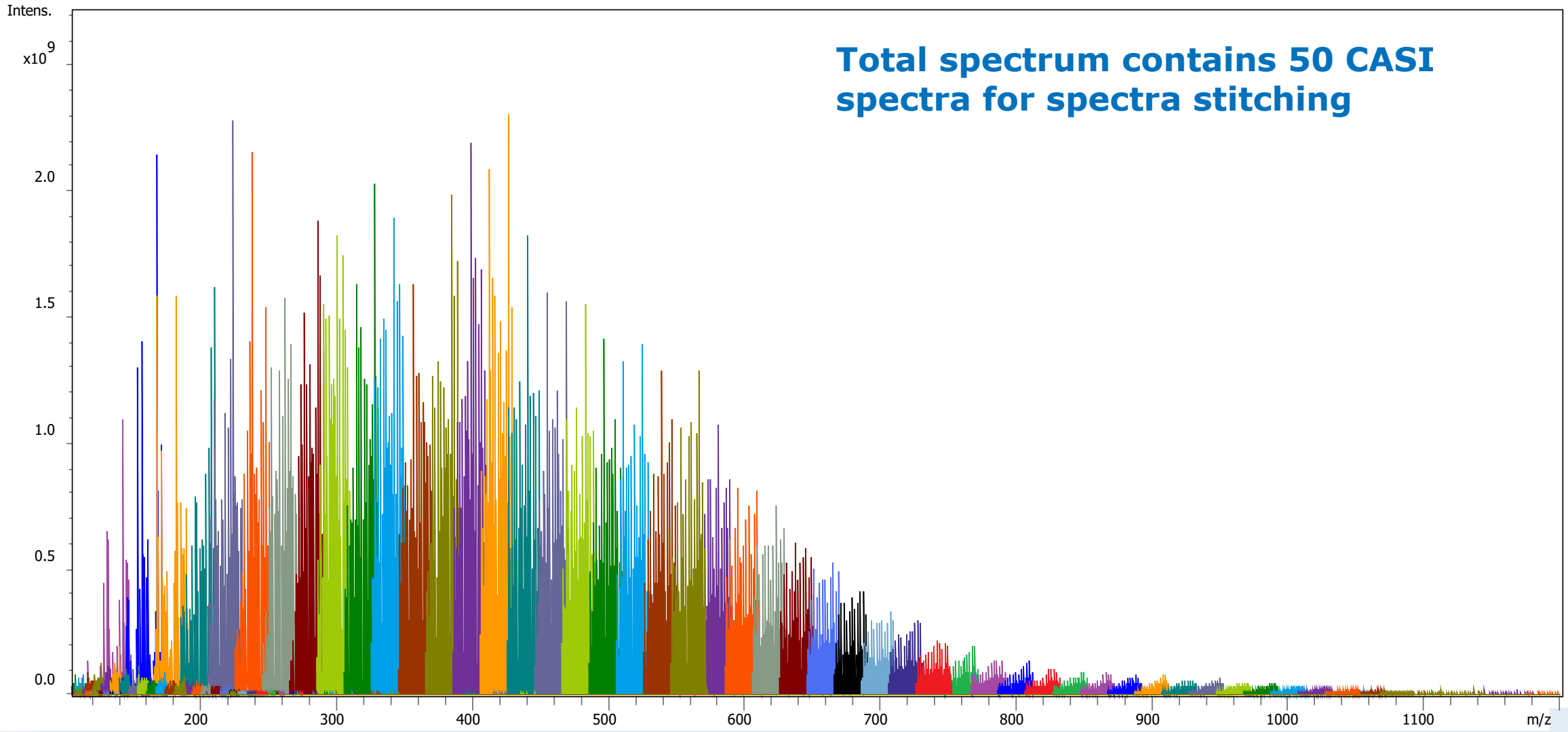
Crude oil spectrum– spectra stitching

Stitched spectrum (APPI pos) – North sea crude oil



Crude oil spectrum– spectra stitching

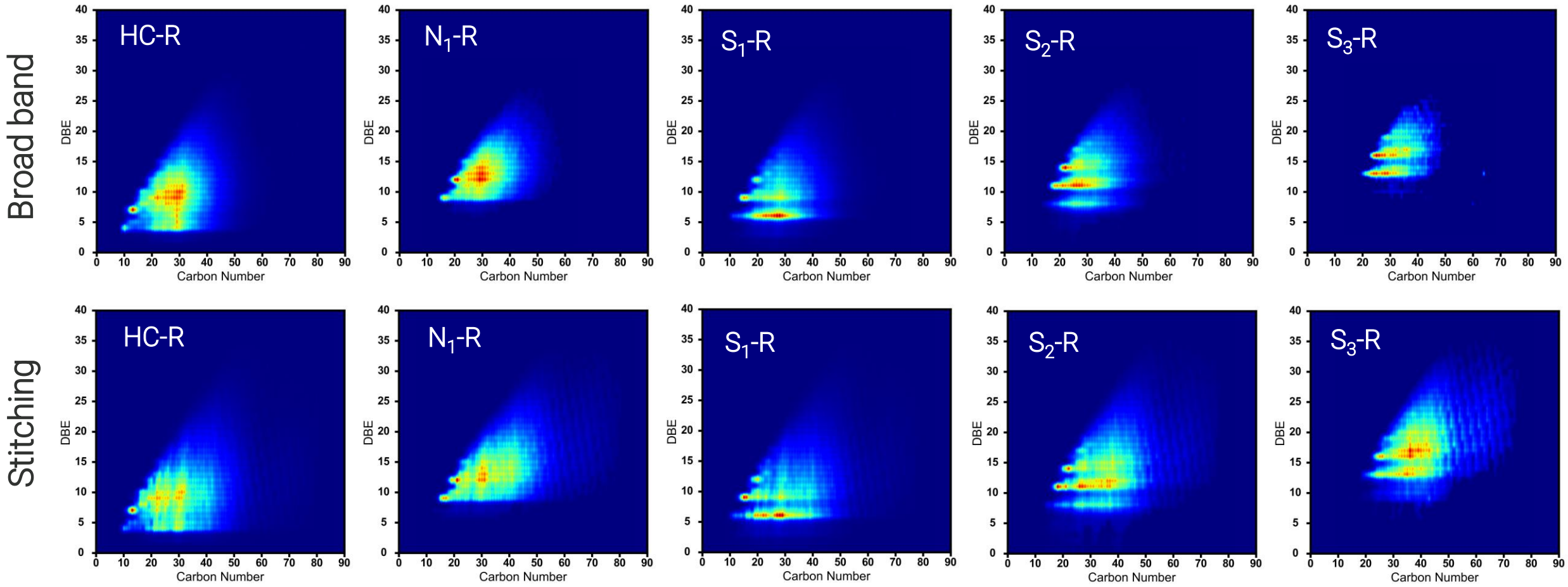
Stitched spectrum (APPI pos) – North sea crude oil



Total spectrum contains 50 CASI spectra for spectra stitching

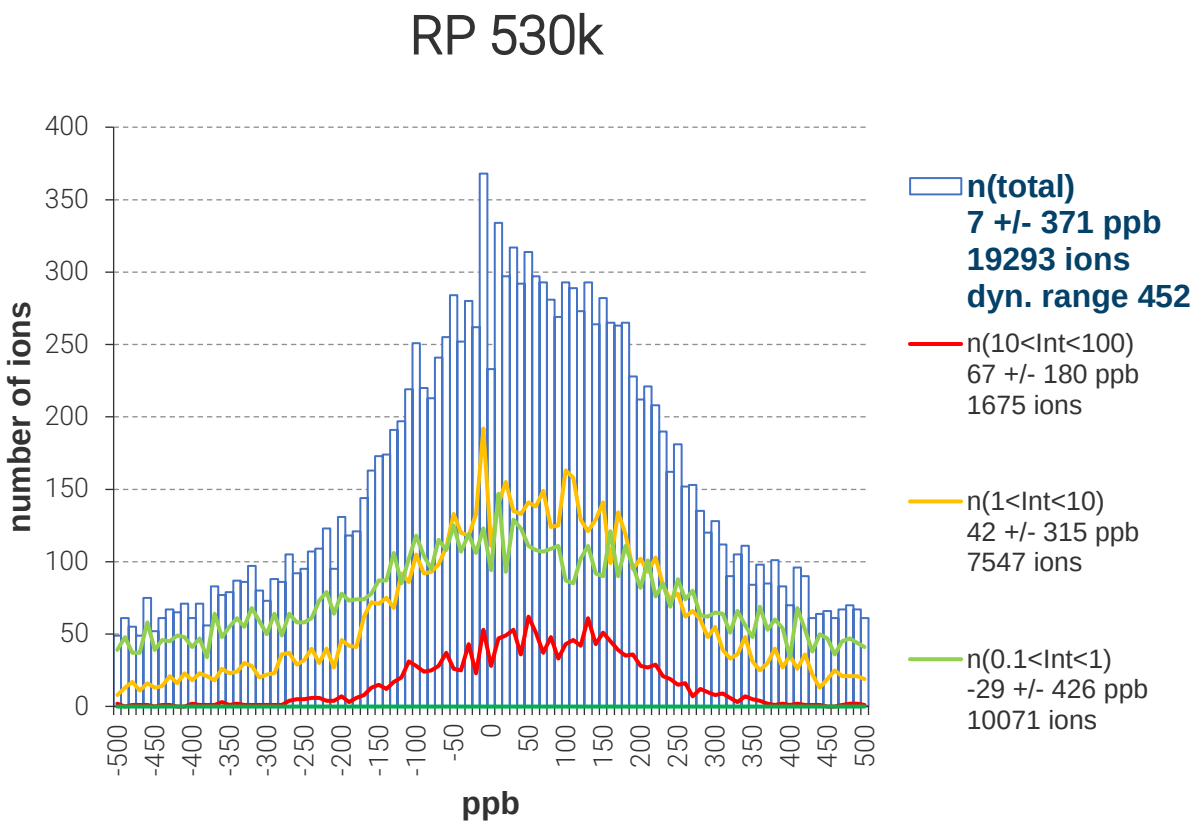
Crude oil results – class plots

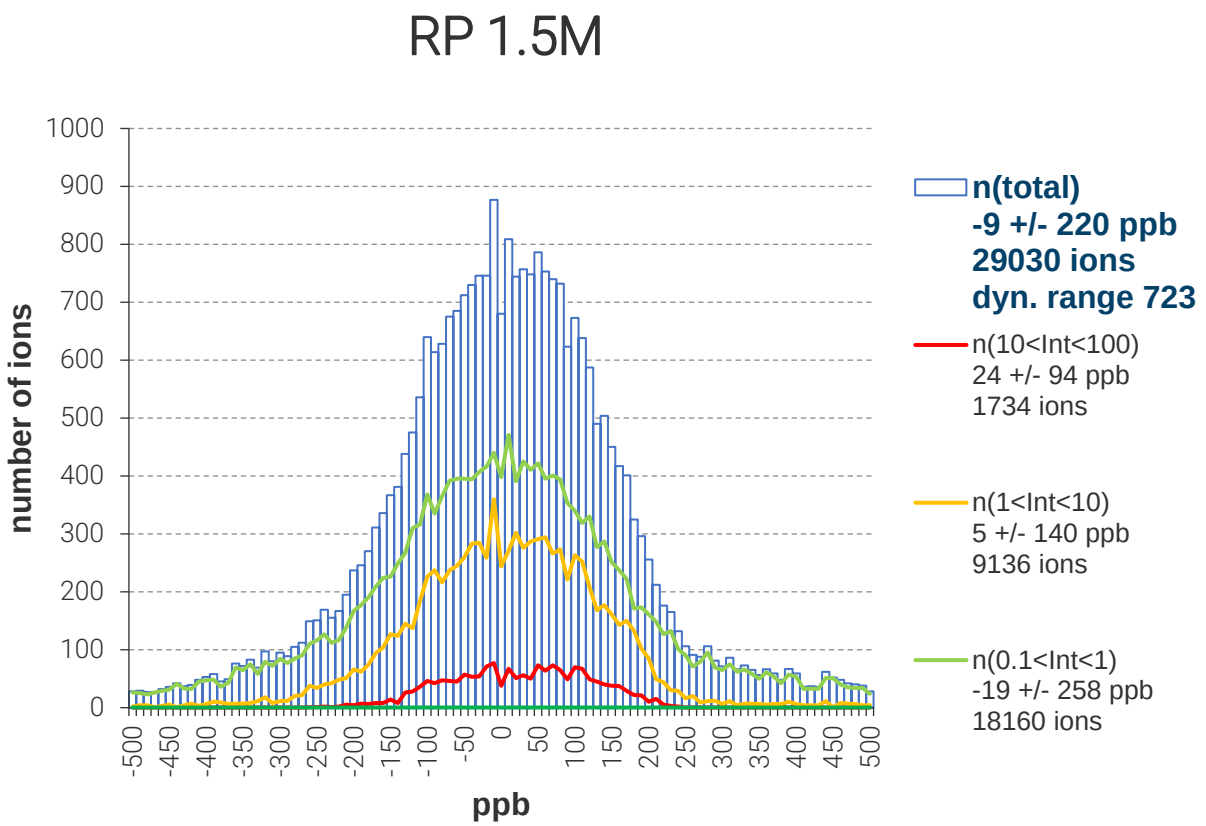
Broadband and stitching spectra results (APPI pos)



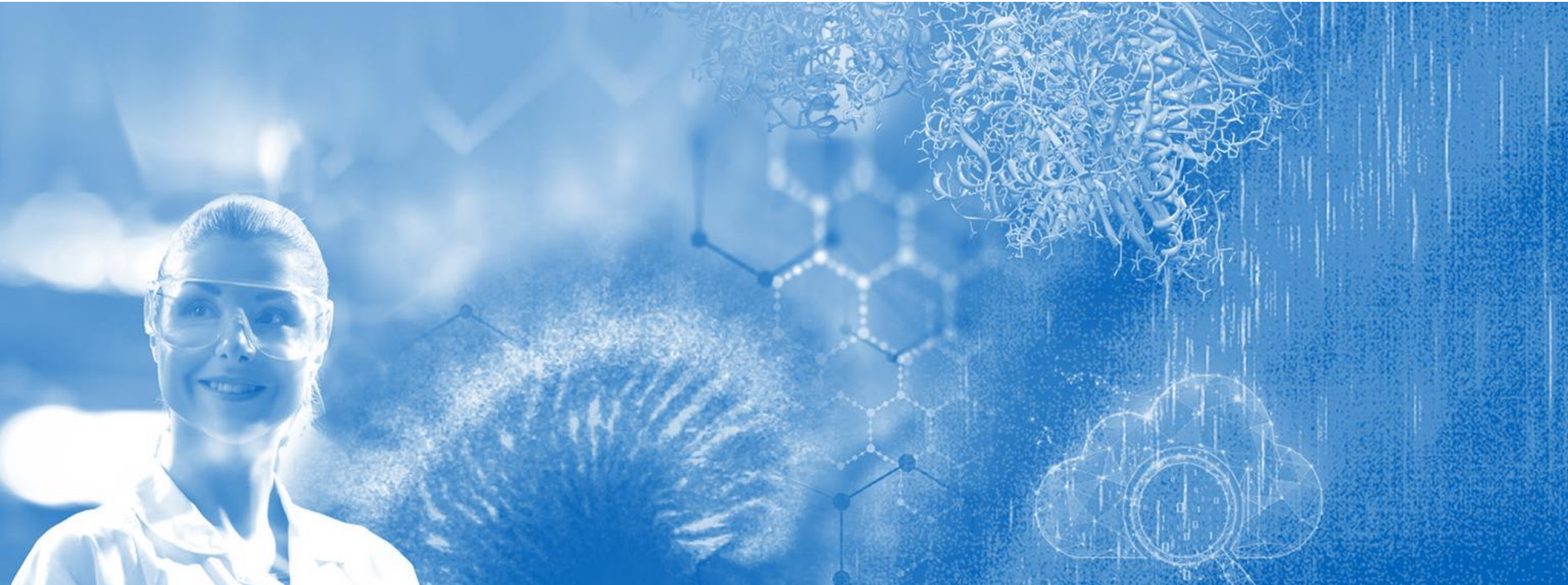
Crude oil results – mass error plots

Broadband (left) and stitching spectra results (right)

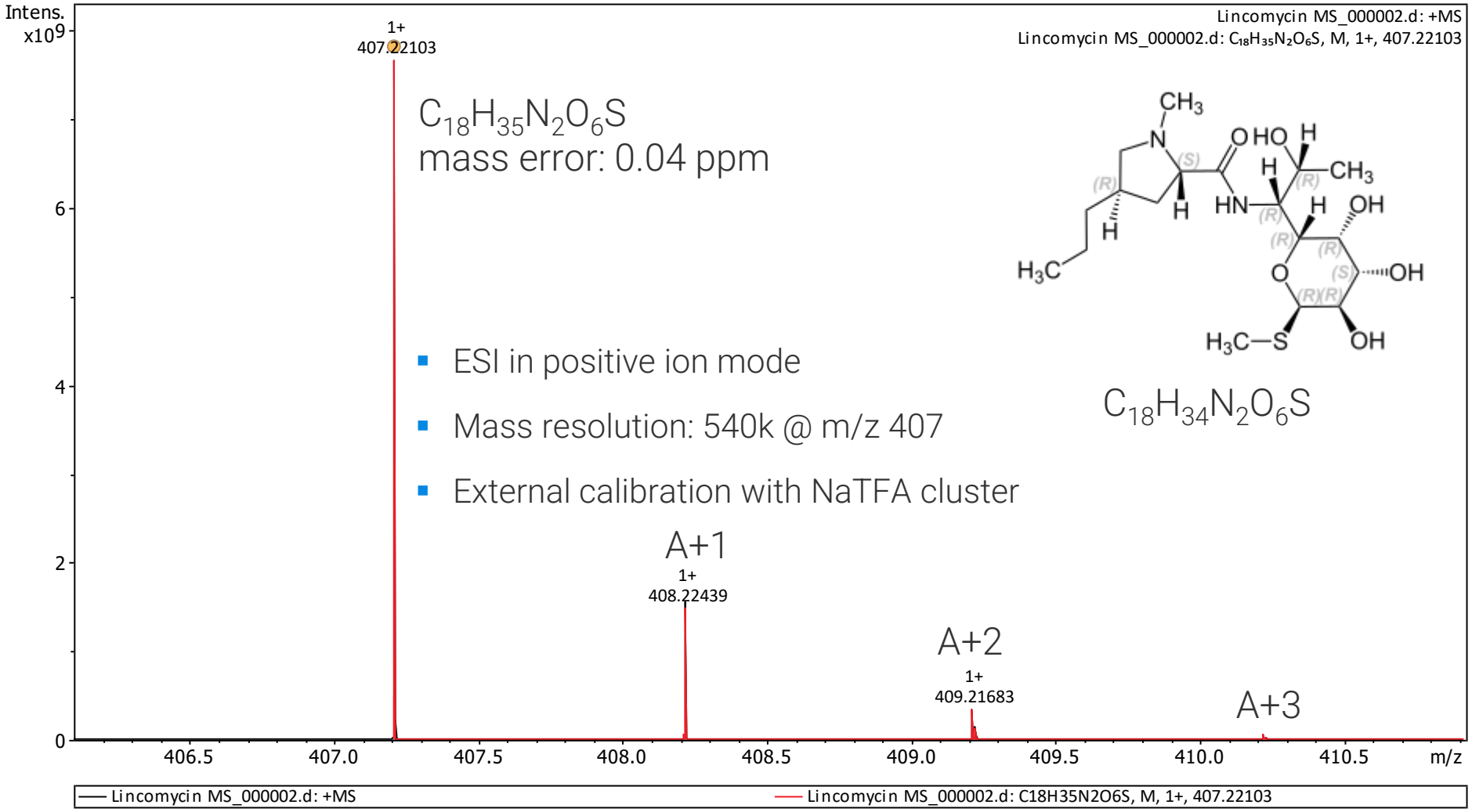




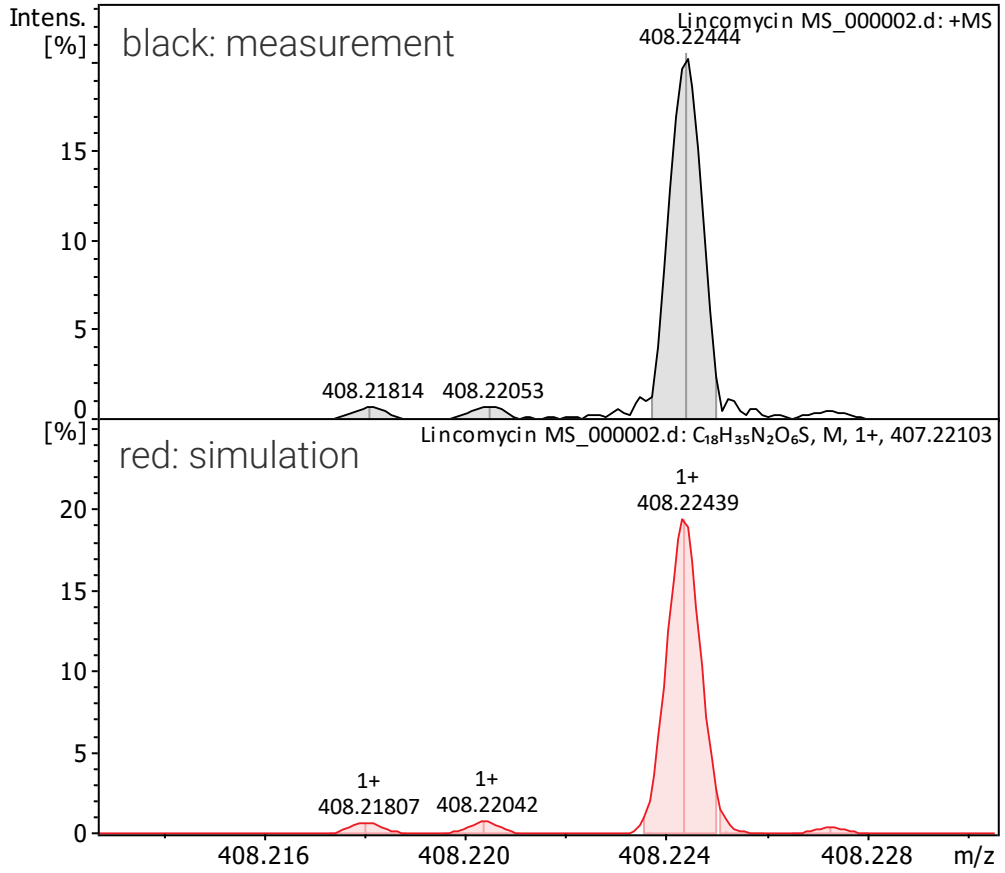
Application of ultra-high mass resolution: Isotopic fine structure

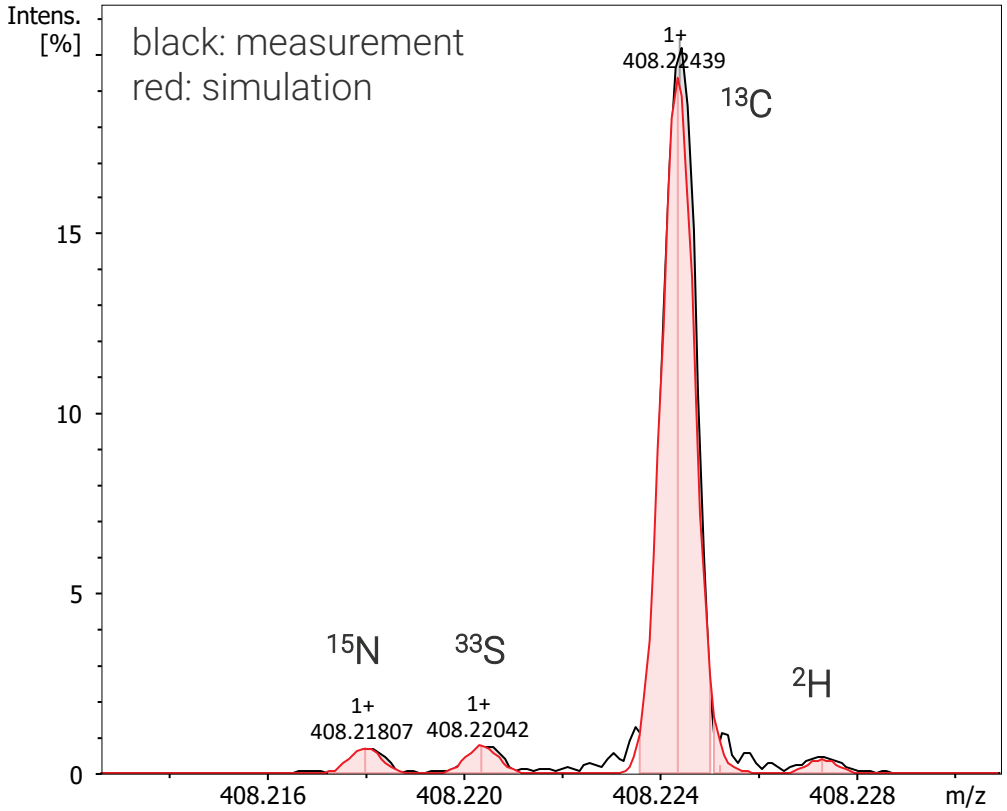


Molecular formula verification

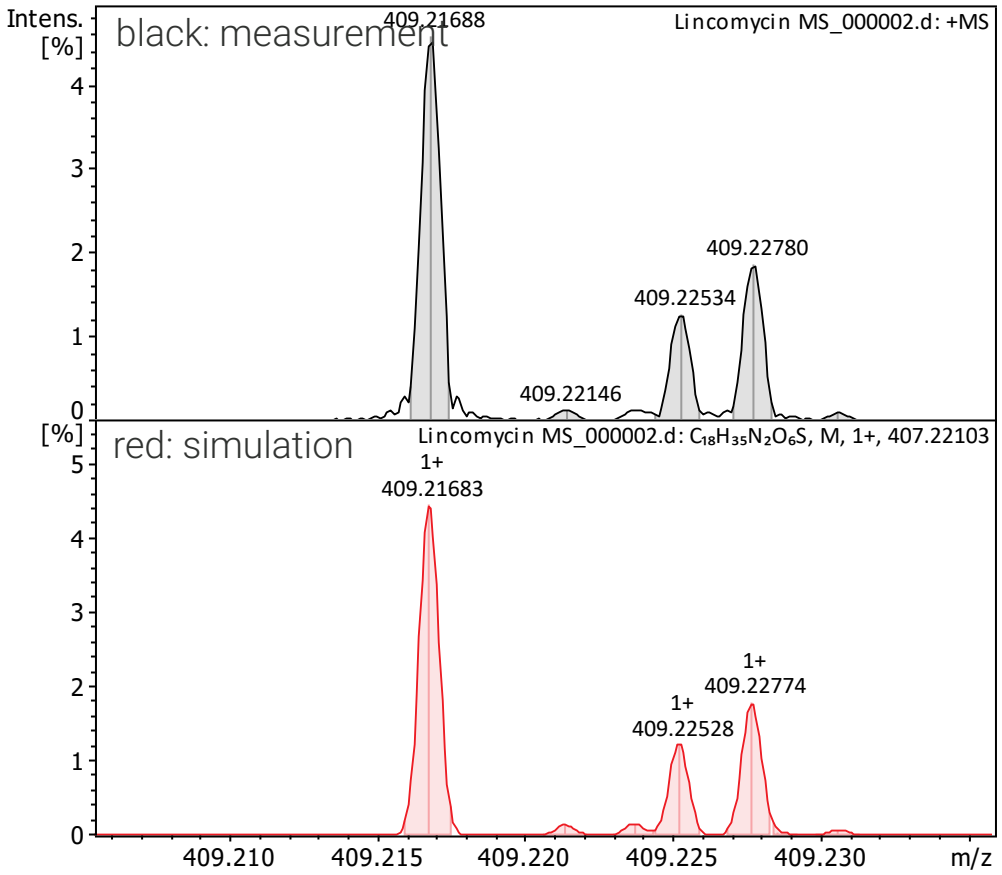


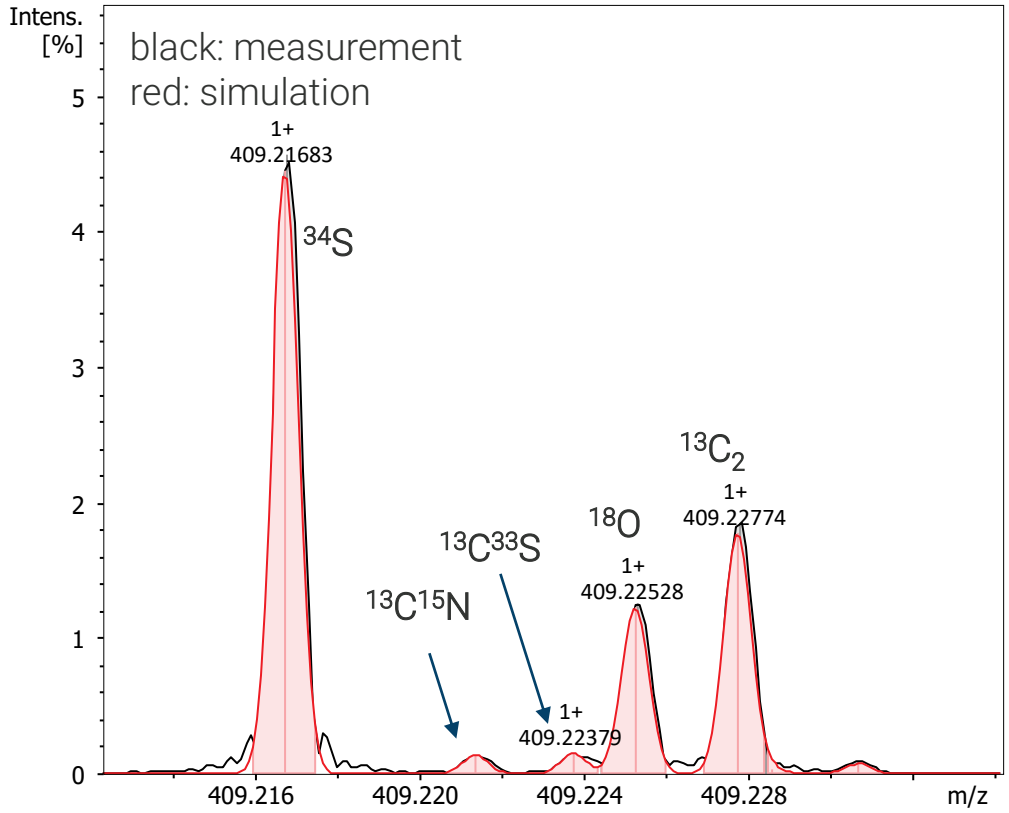
Molecular formula verification
IFS of Lincomycin – A+1 pattern



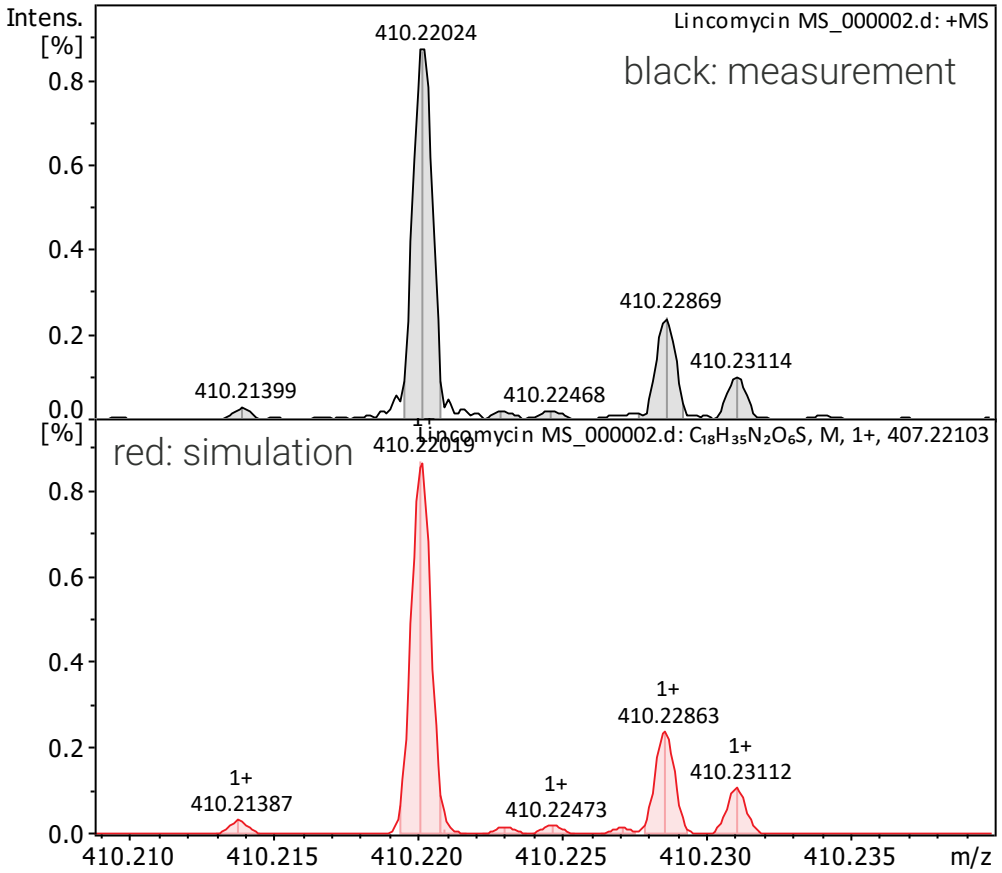


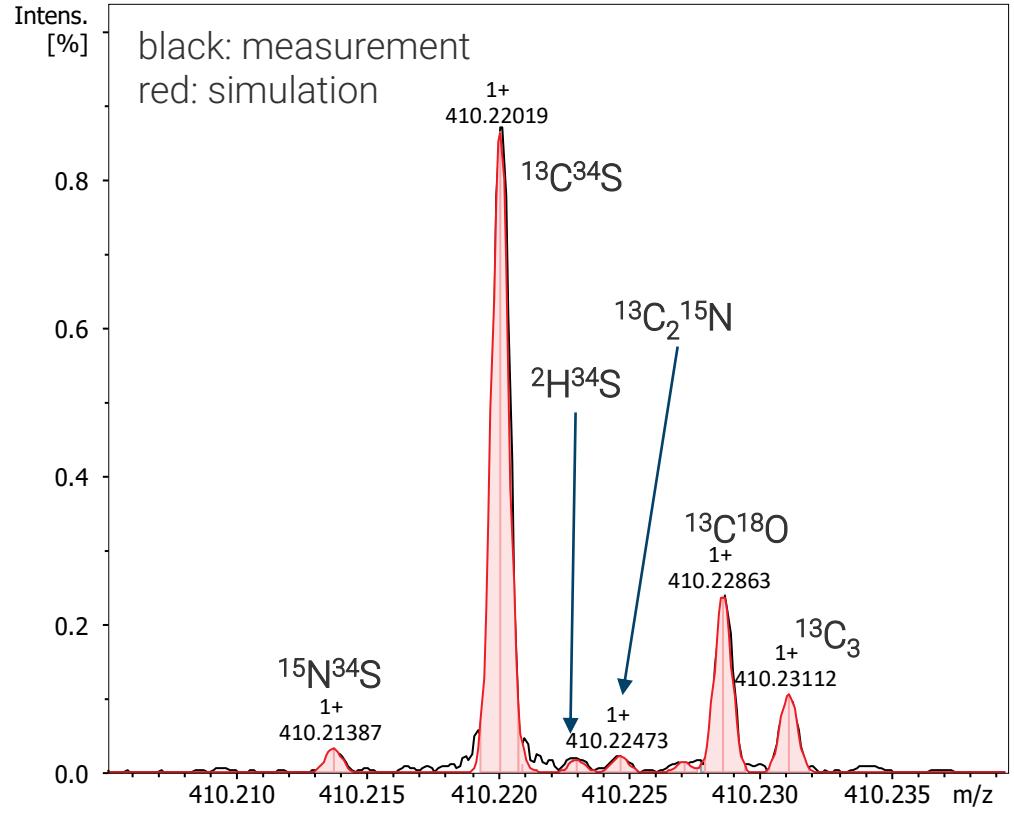
Molecular formula verification
IFS of Lincomycin – A+2 pattern





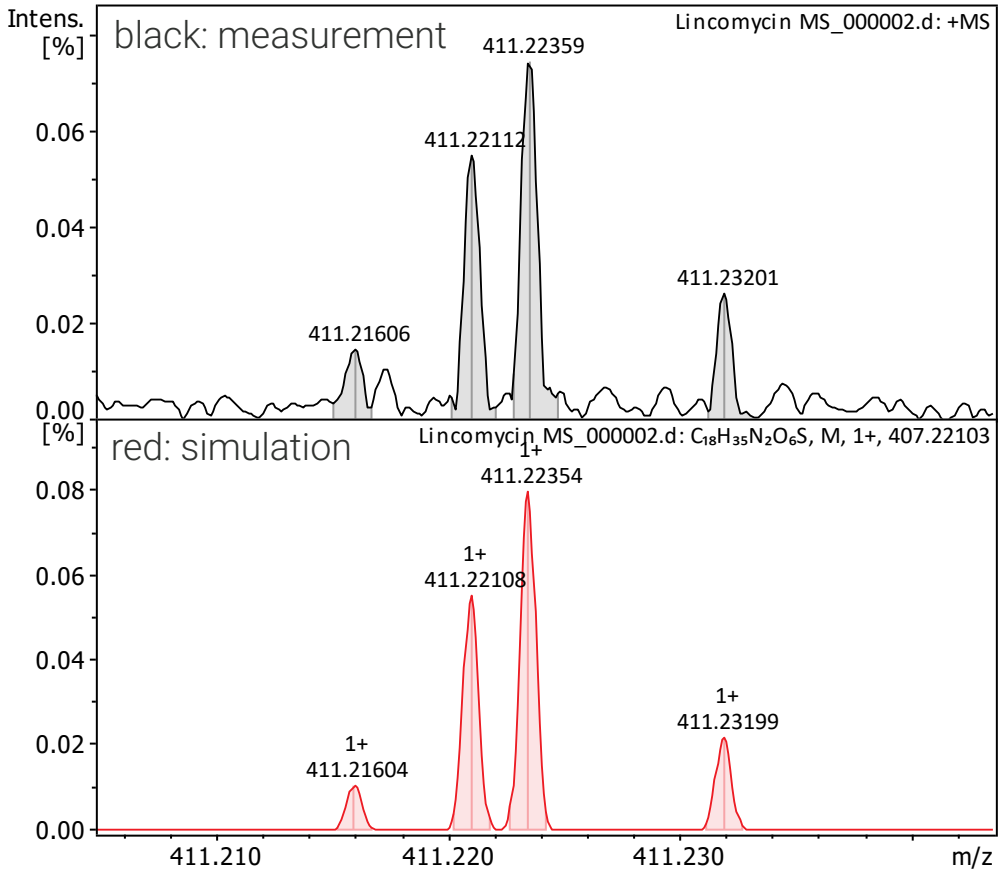
Molecular formula verification
IFS of Lincomycin – A+3 pattern

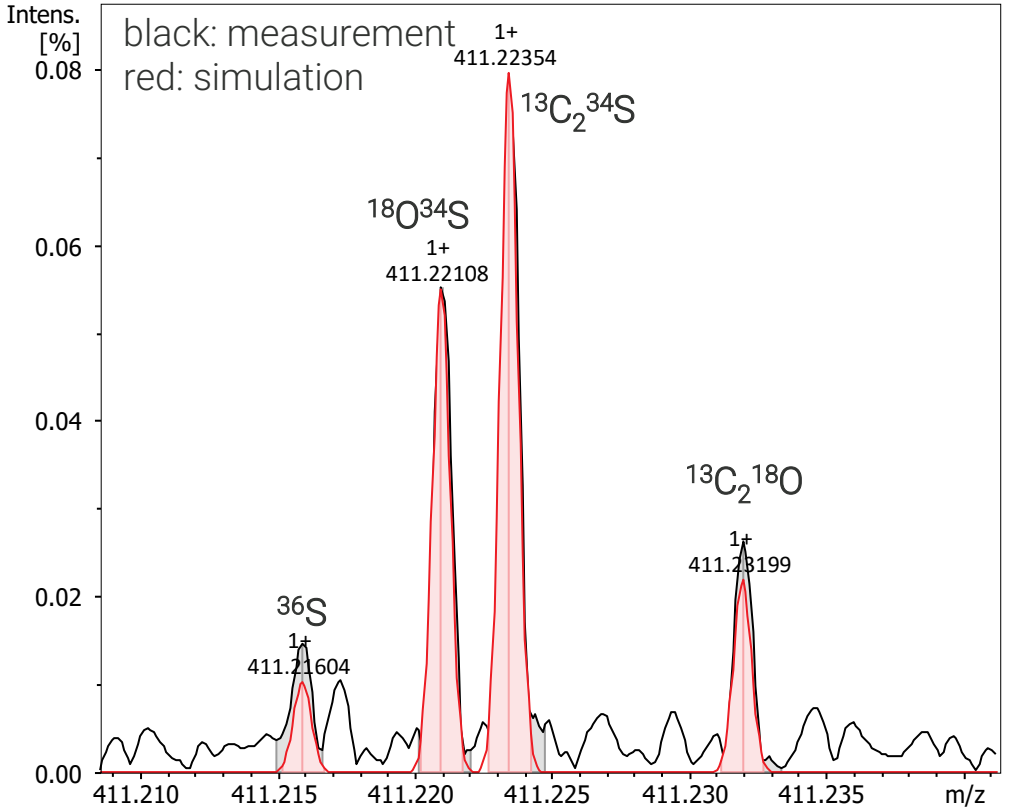




Innovation with Integrity 6 January 2023 43

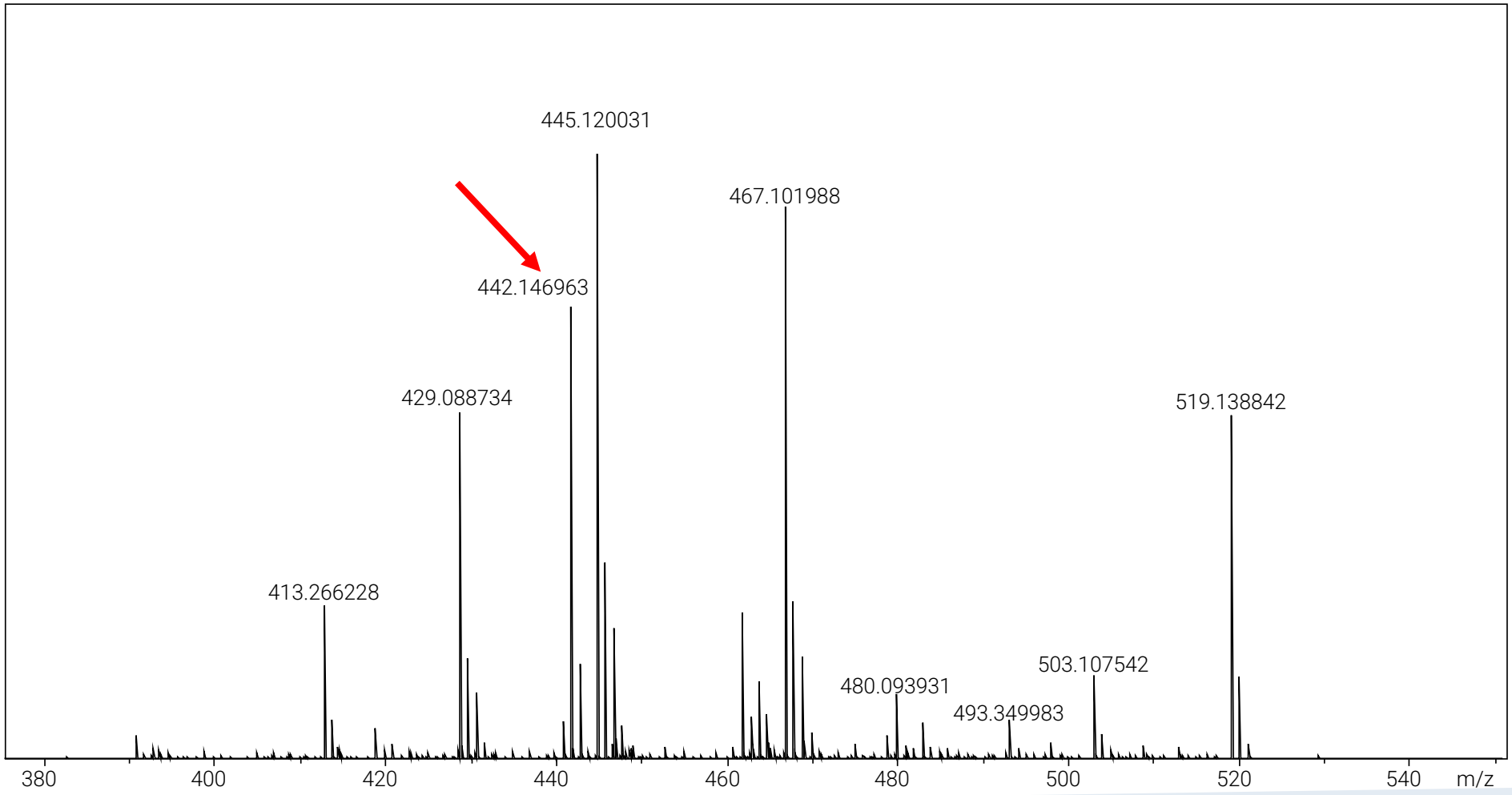
Molecular formula verification
IFS of Lincomycin – A+4 pattern





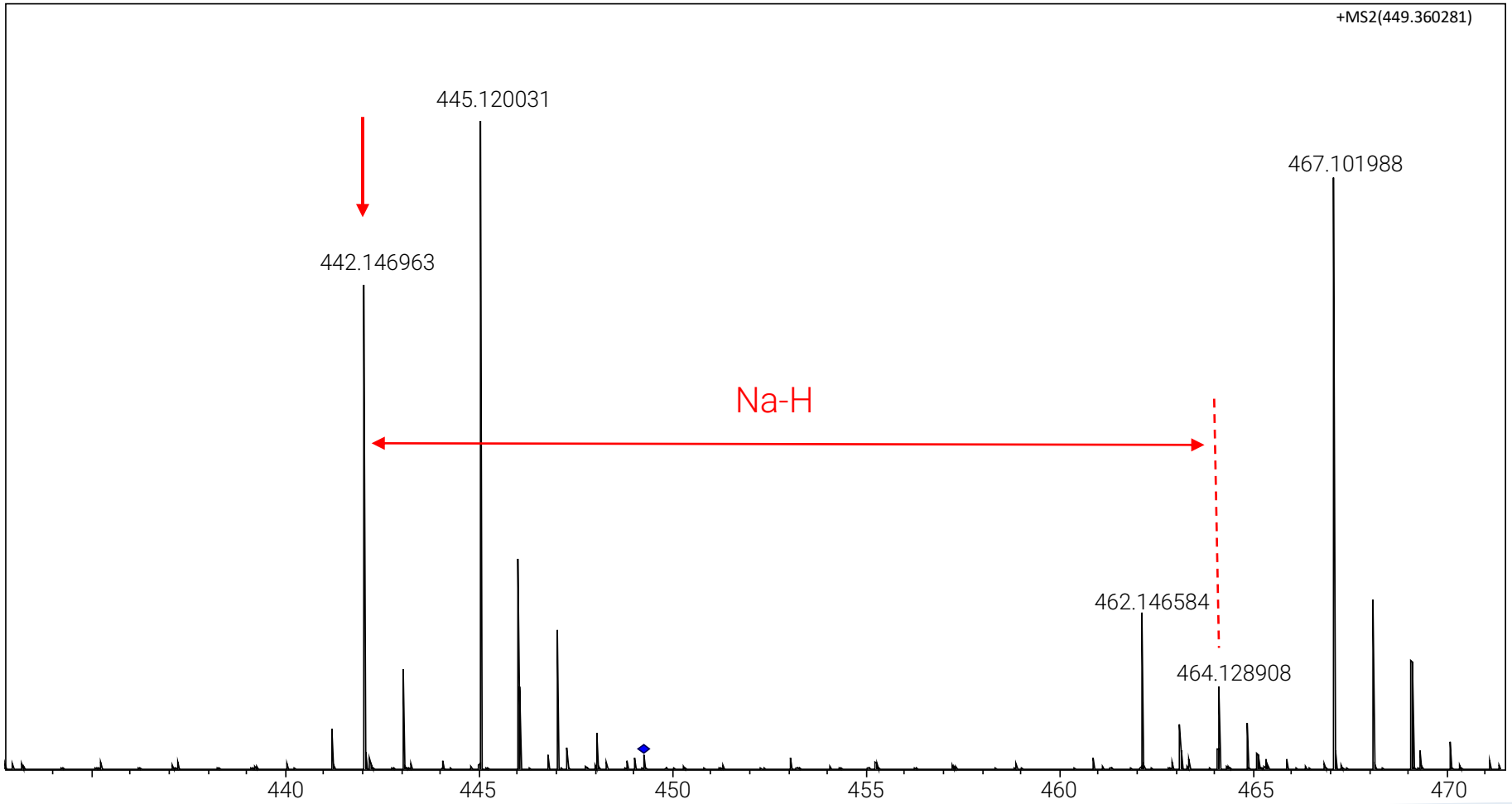
Molecular formula elucidation

LC Fraction of plant extract: Identify compound at m/z 442.1469



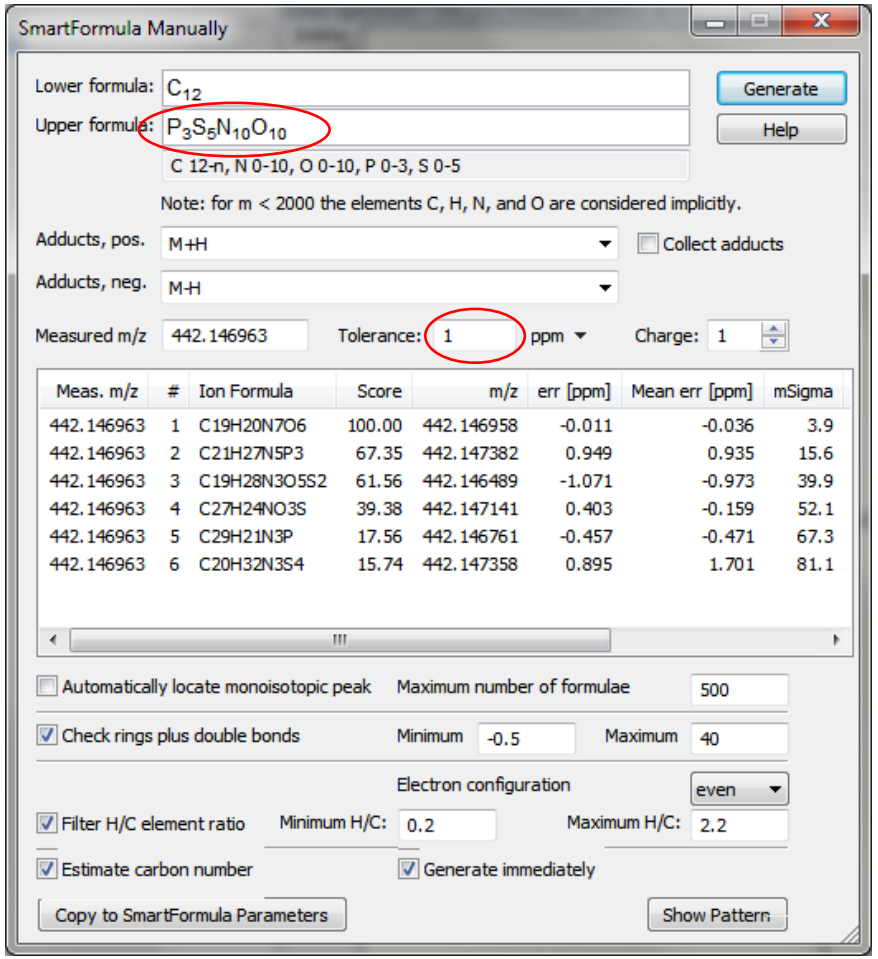
Molecular formula elucidation

LC Fraction of plant extract: Identify compound at m/z 442.1469



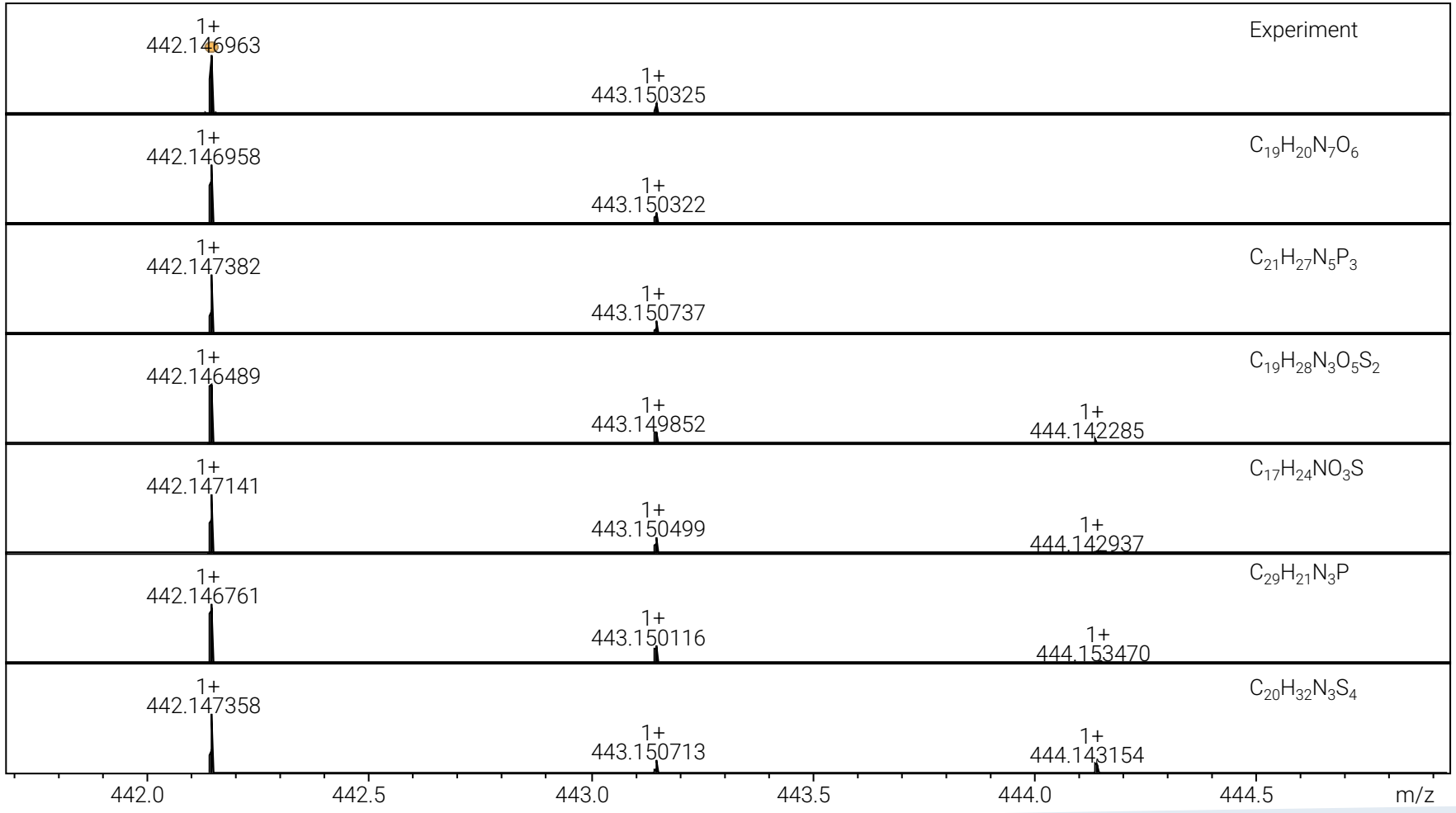
Molecular formula elucidation

LC Fraction of plant extract: Identify compound at m/z 442.1469



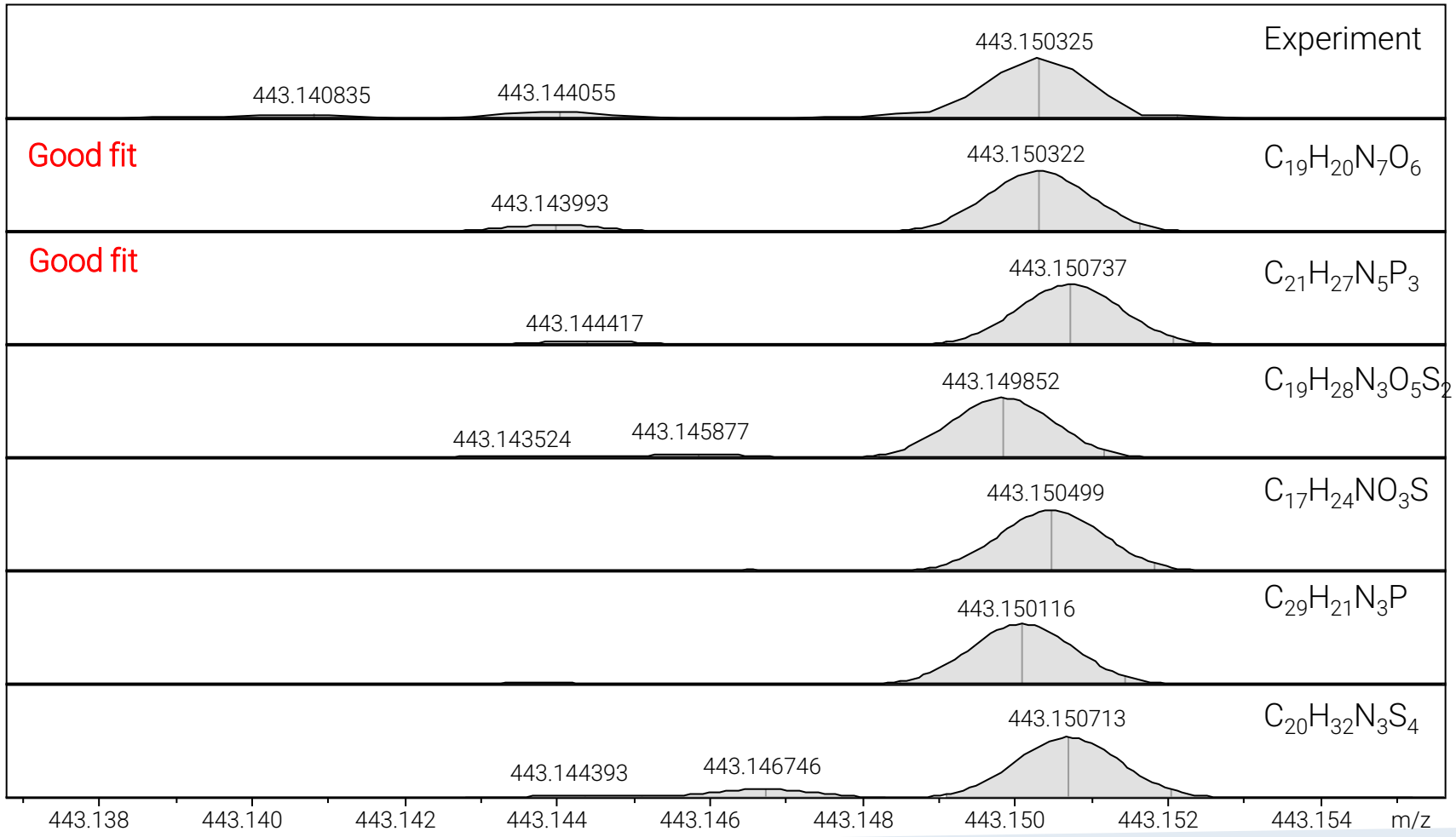
Molecular formula elucidation

LC Fraction of plant extract: Identify compound at m/z 442.1469



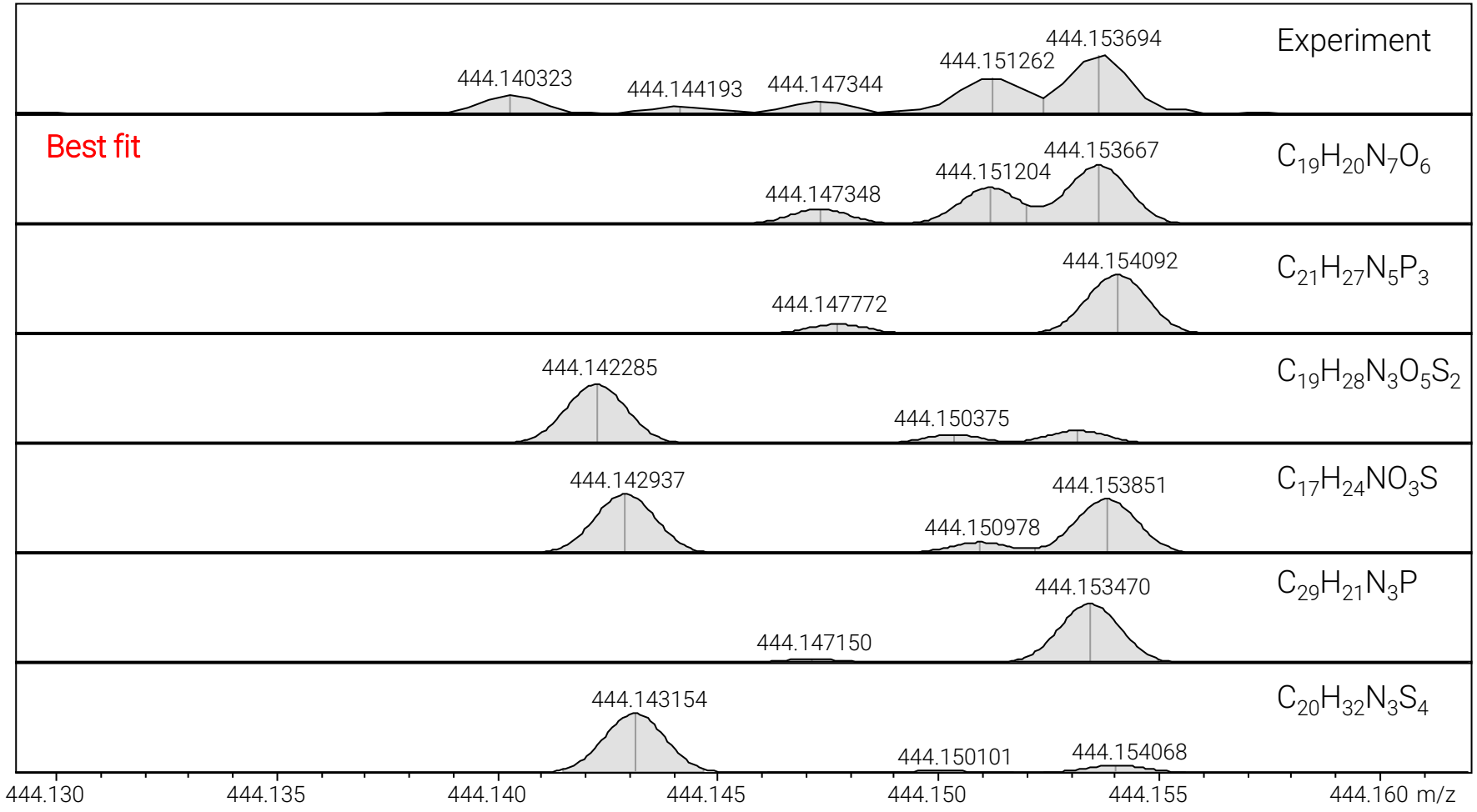
Molecular formula elucidation

LC Fraction of plant extract: Check isotopic fine structure of A+1 pattern



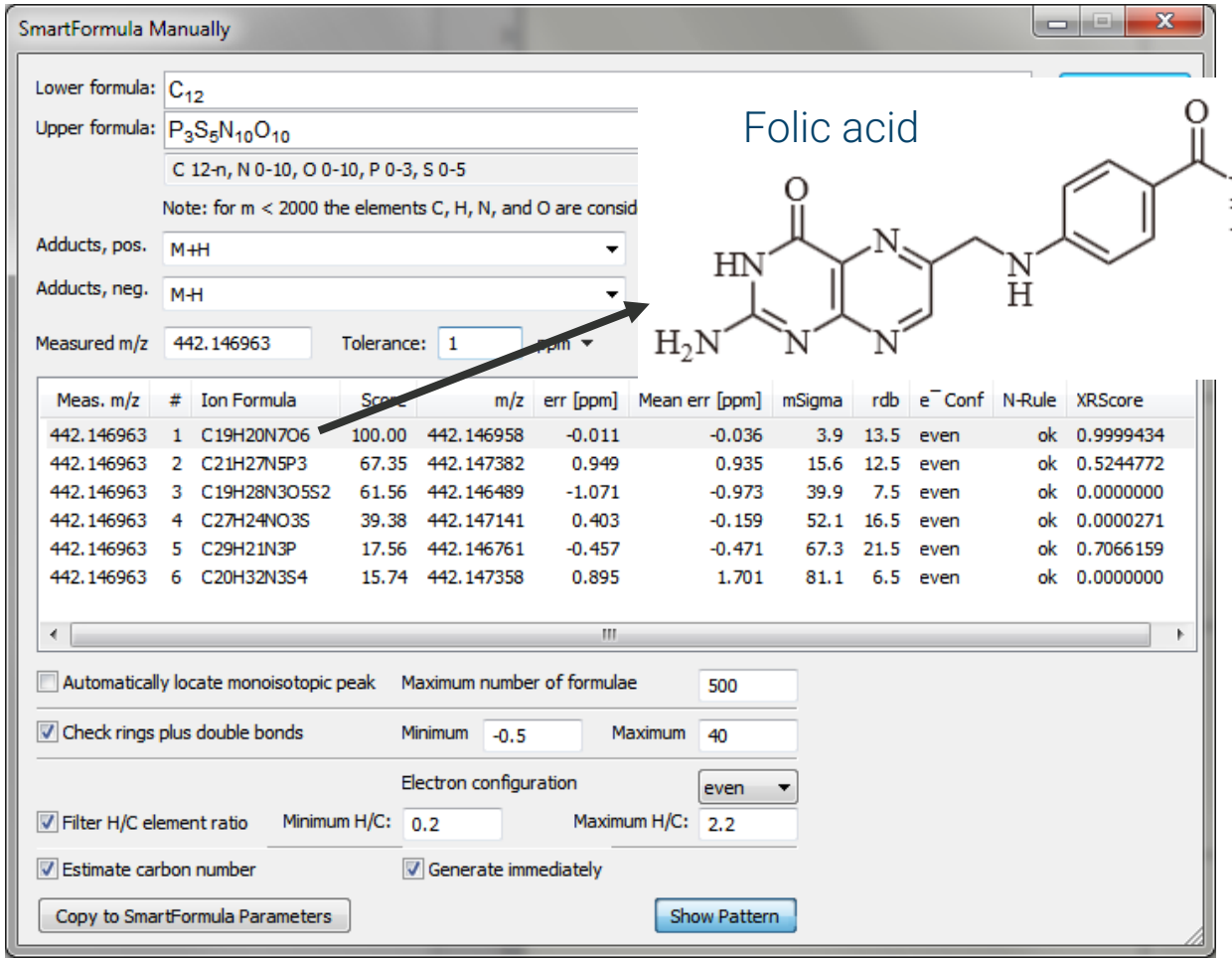
Molecular formula elucidation

LC Fraction of plant extract: Check isotopic fine structure of A+2 pattern



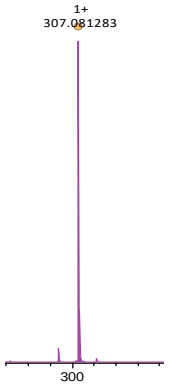
Molecular formula elucidation

LC Fraction of plant extract: Check isotopic fine structure of A+2 pattern

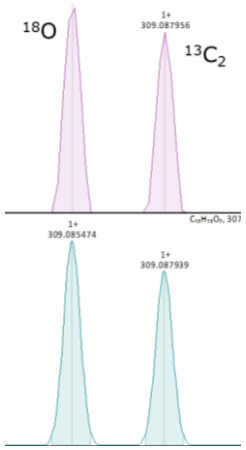


Isotpoic fine structure in LCMS (2ω detection)

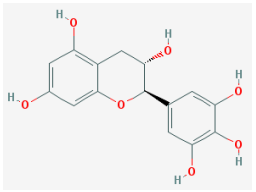
Resolution
600k @m/z 307
Mass error
175 ppb



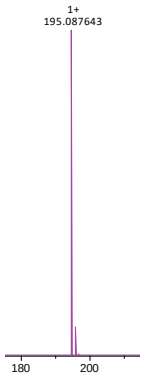
IFS of
A+2 peak



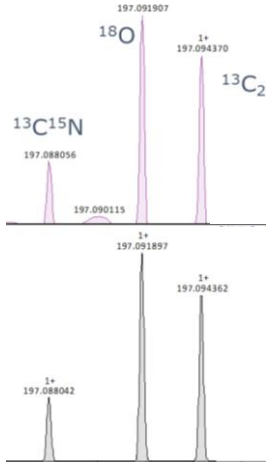
Detection of
Gallocatechin



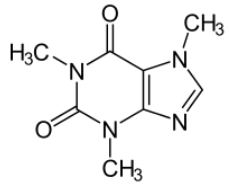
Resolution
980k @m/z 195
Mass error
47 ppb



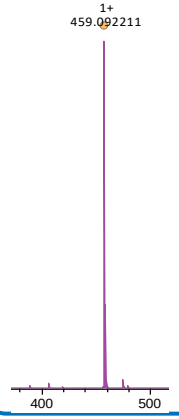
IFS of
A+2 peak



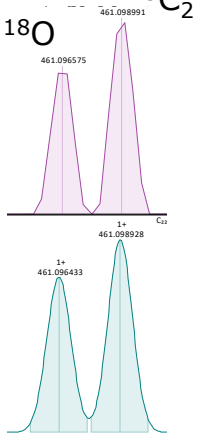
Detection of
Caffeine



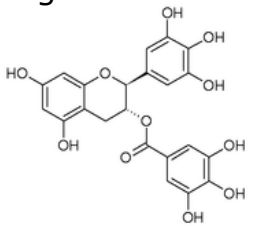
Resolution
400k @m/z 459
Mass error
51 ppb



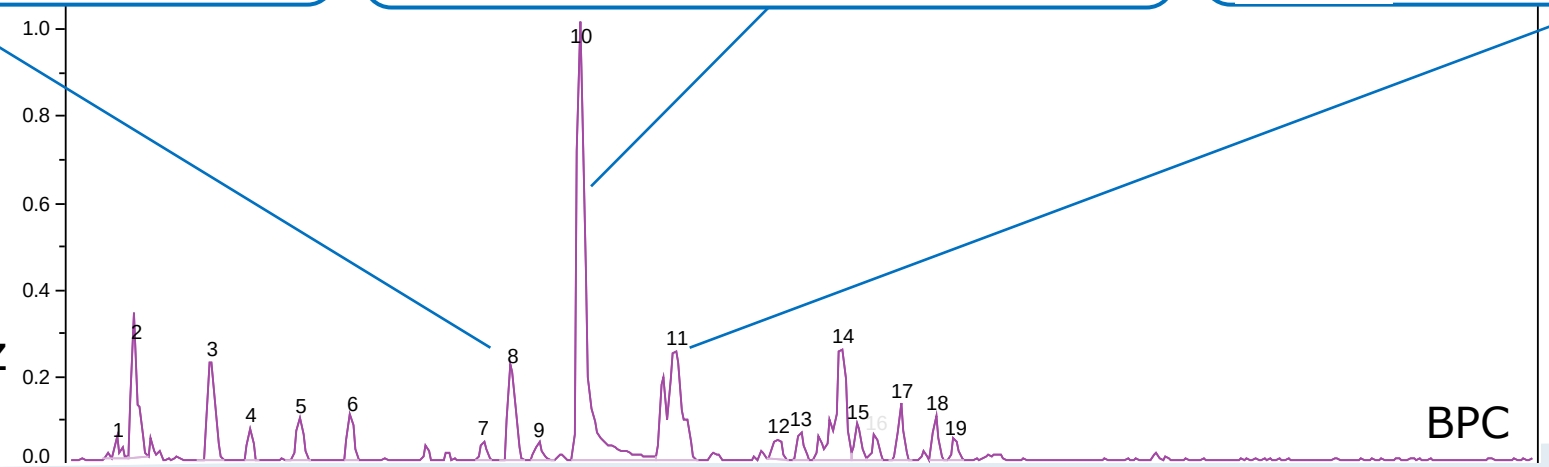
IFS of
A+2 peak



Detection of
Epigallo-
catechin
gallate

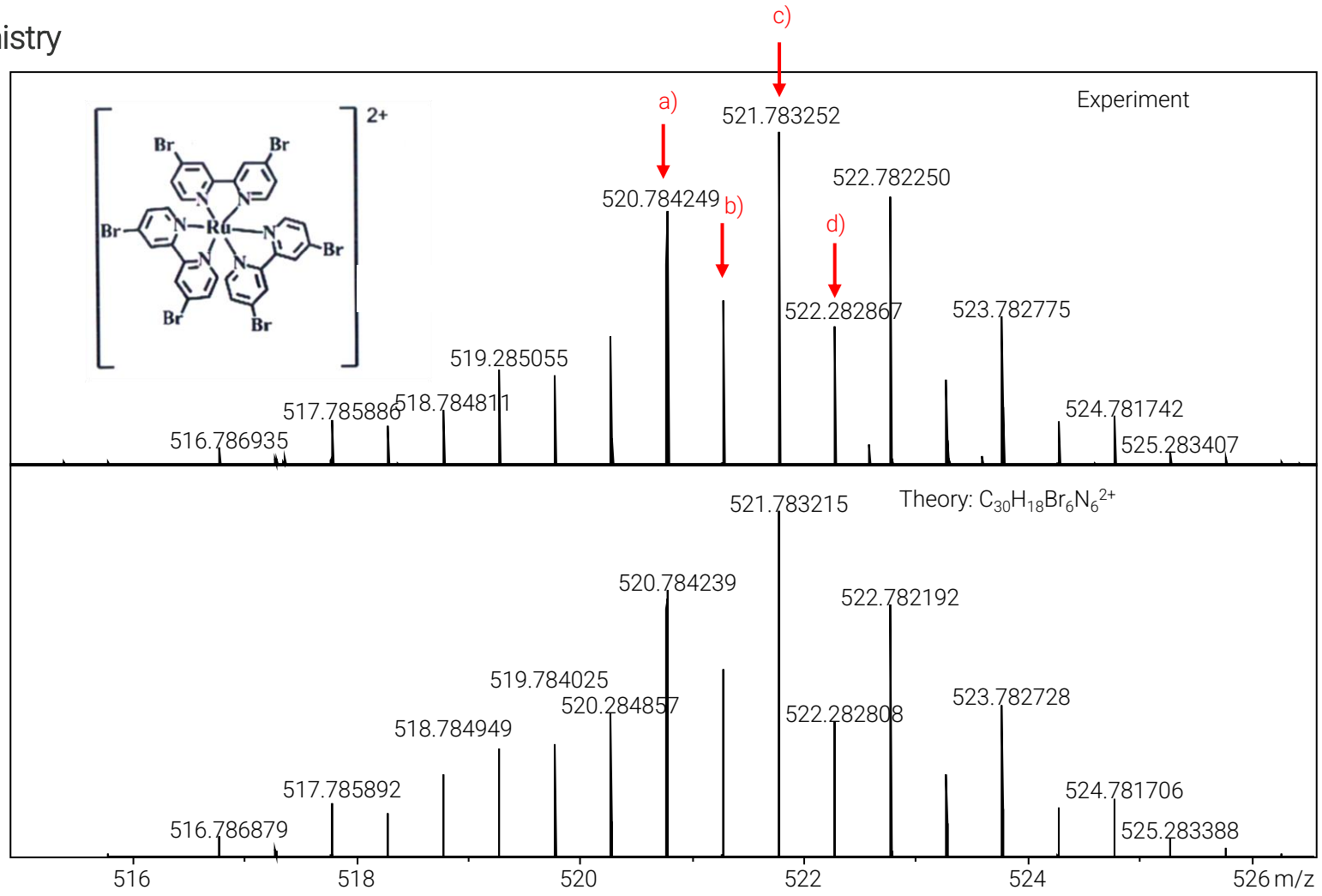


LCMS-ESI(+)
Darjeeling tea, 1Hz
Bruker **scimaX**



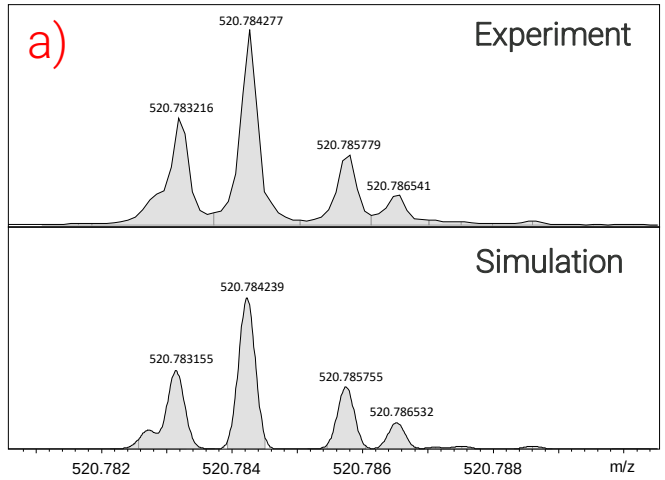
Complex isotopic distribution and isotopic fine structure

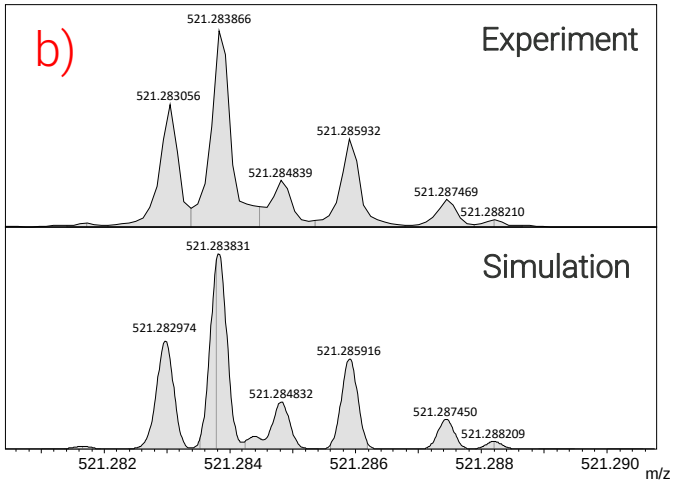
Metal organic chemistry

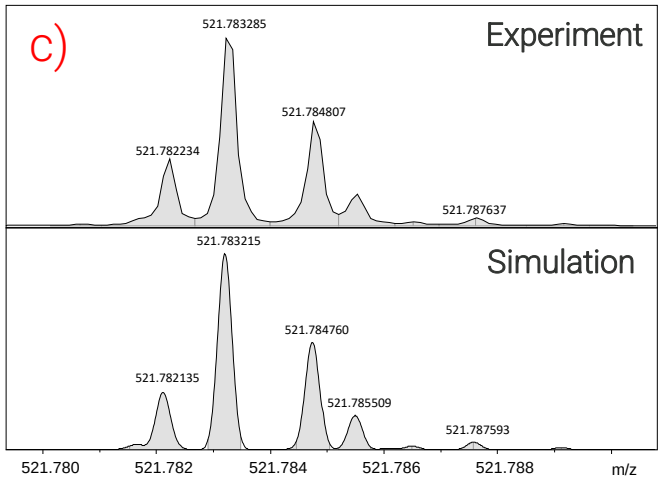


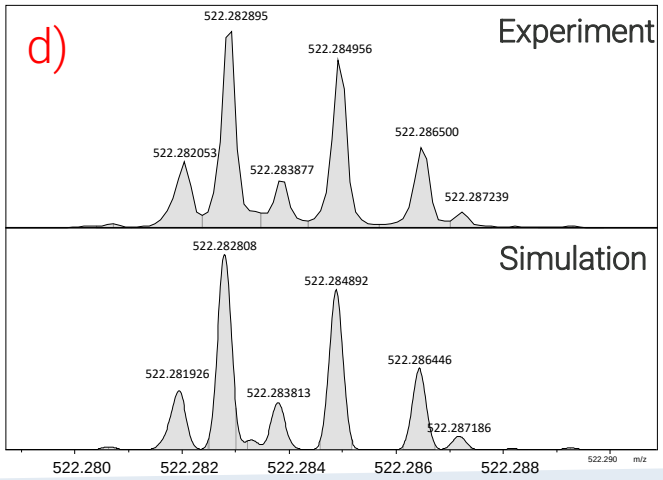
Complex isotopic distribution and isotopic fine structure

Metal organic chemistry





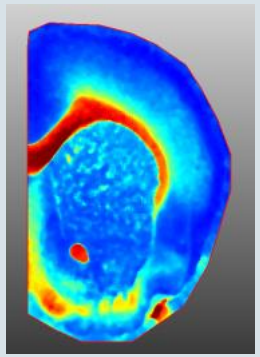




Summary of MRMS Applications

MRMS

- Complex mixture analysis (Petroleomics, NOM, etc.)
- Small molecules and Isotopic fine strcuture (IFS)
- Biomolecules (proteins, etc.)
- MALDI Imaging (lipids, peptides, proteins with HIPLEX tags, etc.)

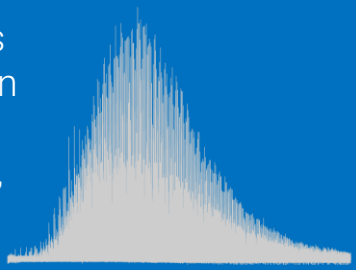


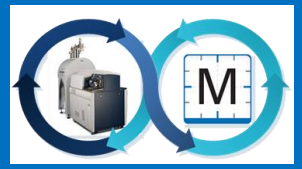
MALDI Imaging

Label-free MALDI imaging maps the localization of drugs and metabolites, providing spatial correlation with 'omics studies

Petroleomics

Exact chemical class information can aid in solving problems in petroleum collection, processing, and transport



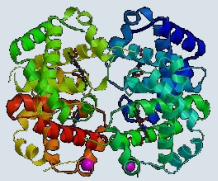


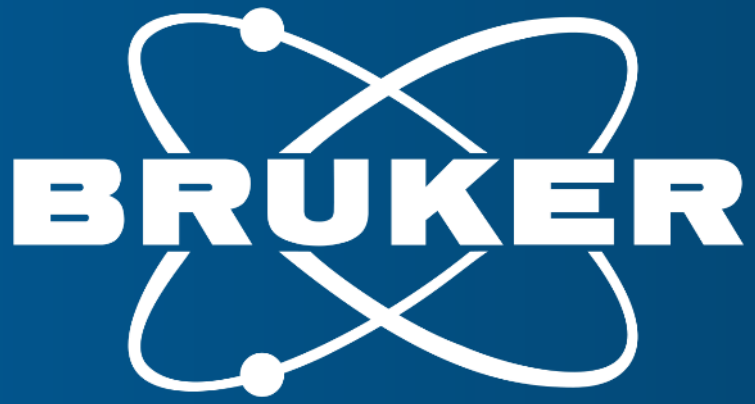
Small Molecules

Flow Injection Analysis (FIA) MRMS workflows accelerate sample throughput and increase data depth in Phenomics research

Intact Biomolecules

Large intact biomolecules can be analyzed for applications in proteomics, biopharmaceutical analysis, and protein science





Innovation with Integrity